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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

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TITLE OF THE INVENTION (500 characters max)

PYRIMIDINYL AMINES AS POTASSIUM ION CHANNEL MODULATORS

Direct all correspondence to: **CORRESPONDENCE ADDRESS**

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ENCLOSED APPLICATION PARTS *(check all that apply)*

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☒ Application Data Sheet. See 37 CFR 1.76

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Respectfully submitted, Date April 13, 2004

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Additional Page

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PROVISIONAL

PATENT APPLICATION

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PYRIDINYL AMINES AS POTASSIUM ION CHANNEL MODULATORS

BACKGROUND OF THE INVENTION

[0001] Ion channels are cellular proteins that regulate the flow of ions, including calcium, potassium, sodium and chloride into and out of cells. These channels are present in all human cells and affect such physiological processes as nerve transmission, muscle contraction, cellular secretion, regulation of heartbeat, dilation of arteries, release of insulin, and regulation of renal electrolyte transport. Among the ion channels, potassium ion channels are the most ubiquitous and diverse, being found in a variety of animal cells such as nervous, muscular, glandular, immune, reproductive, and epithelial tissue. These channels allow the flow of potassium in and/or out of the cell under certain conditions. For example, the outward flow of potassium ions upon opening of these channels makes the interior of the cell more negative, counteracting depolarizing voltages applied to the cell. These channels are regulated, *e.g.*, by calcium sensitivity, voltage-gating, second messengers, extracellular ligands, and ATP-sensitivity.

[0002] Potassium ion channels are typically formed by four alpha subunits, and can be homomeric (made of identical alpha subunits) or heteromeric (made of two or more distinct types of alpha subunits). In addition, certain potassium ion channels (those made from Kv, KQT and Slo or BK subunits) have often been found to contain additional, structurally distinct auxiliary, or beta subunits. These subunits do not form potassium ion channels themselves, but instead they act as auxiliary subunits to modify the functional properties of channels formed by alpha subunits. For example, the Kv beta subunits are cytoplasmic and are known to increase the surface expression of Kv channels and/or modify inactivation kinetics of the channel (Heinemann *et al.*, *J. Physiol.* **493**: 625-633 (1996); Shi *et al.*, *Neuron* **16**(4): 843-852 (1996)). In another example, the KQT family beta subunit, minK, primarily changes activation kinetics (Sanguinetti *et al.*, *Nature* **384**: 80-83 (1996)).

[0003] The alpha subunits of potassium ion channels fall into at least 8 families, based on predicted structural and functional similarities (Wei *et al.*, *Neuropharmacology* **35(7)**: 805-829 (1997)). Three of these families (Kv, eag-related, and KQT) share a common motif of six transmembrane domains and are primarily gated by voltage. Two other families, CNG and SK/IK, also contain this motif but are gated by cyclic nucleotides and calcium,

respectively. Small (SK) and intermediate (IK) conductance calcium-activated potassium ion channels possess unit conductances of 2-20 and 20-85 pS, respectively, and are more sensitive to calcium than are BK channels discussed below. For a review of calcium-activated potassium channels see Latorre *et al.*, *Ann. Rev. Phys.* **51**: 385-399 (1989).

[0004] Three other families of potassium channel alpha subunits have distinct patterns of transmembrane domains. Slo or BK family potassium channels have seven transmembrane domains (Meera *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **94(25)**: 14066-14071 (1997)) and are gated by both voltage and calcium or pH (Schreiber *et al.*, *J. Biol. Chem.* **273**: 3509-3516 (1998)). Slo or BK potassium ion channels are large conductance potassium ion channels found in a wide variety of tissues, both in the central nervous system and periphery. These channels are gated by the concerted actions of internal calcium ions and membrane potential, and have a unit conductance between 100 and 220 pS. They play a key role in the regulation of processes such as neuronal integration, muscular contraction and hormone secretion. They may also be involved in processes such as lymphocyte differentiation and cell proliferation, spermatocyte differentiation and sperm motility. Members of the BK (Atkinson *et al.*, *Science* **253**: 551-555 (1991); Adelman *et al.*, *Neuron* **9**: 209-216 (1992); Butler, *Science* **261**: 221-224 (1993)) subfamily have been cloned and expressed in heterologous cell types where they recapitulate the fundamental properties of their native counterparts. Finally, the inward rectifier potassium channels (Kir), belong to a structural family containing two transmembrane domains, and an eighth functionally diverse family (TP, or "two-pore") contains two tandem repeats of this inward rectifier motif.

[0005] Each type of potassium ion channel shows a distinct pharmacological profile. These classes are widely expressed, and their activity hyperpolarizes the membrane potential. Potassium ion channels have been associated with a number of physiological processes, including regulation of heartbeat, dilation of arteries, release of insulin, excitability of nerve cells, and regulation of renal electrolyte transport. Moreover, studies have indicated that potassium ion channels are a therapeutic target in the treatment of a number of diseases including central or peripheral nervous system disorders (*e.g.*, migraine, ataxia, Parkinson's disease, bipolar disorders, trigeminal neuralgia, spasticity, mood disorders, brain tumors, psychotic disorders, myokymia, seizures, epilepsy, hearing and vision loss, psychosis, anxiety, depression, dementia, memory and attention deficits, Alzheimer's disease, age-related memory loss, learning deficiencies, anxiety, traumatic brain injury, dysmenorrhea, narcolepsy and motor neuron diseases), as well as targets for neuroprotective agents (*e.g.*, to

prevent stroke and the like); as well as disease states such as gastroesophogeal reflux disorder and gastrointestinal hypomotility disorders, irritable bowel syndrome, secretory diarrhea, asthma, cystic fibrosis, chronic obstructive pulmonary disease and rhinorrhea, convulsions, vascular spasms, coronary artery spasms, renal disorders, polycystic kidney disease, bladder spasms, urinary incontinence, bladder outflow obstruction, ischemia, cerebral ischemia, ischemic heart disease, angina pectoris, coronary heart disease, Reynaud's disease, intermittent claudication, Sjorgren's syndrome, arrhythmia, hypertension, myotonic muscle dystrophia, xerostomia, diabetes type II, hyperinsulinemia, premature labor, baldness, cancer, and immune suppression.

[0006] Specifically, SK channels have been shown to have distinct pharmacological profiles. For example, using patch clamp techniques, the effects of eight clinically relevant psychoactive compounds on SK2 subtype channels were investigated (Dreixler *et al.*, *Eur. J. Pharmacol.* **401**: 1-7 (2000)). The evaluated compounds are structurally related to tricyclic antidepressants and include amitriptyline, carbamazepine, chlorpromazine, cyproheptadine, imipramine, tacrine and trifluperazine. Each of the compounds tested was found to block SK2 channel currents with micromolar affinity. A number of neuromuscular inhibiting agents exist that affect SK channels, *e.g.* apamin, atracurium, pancuronium and tubocurarine (Shah *et al.*, *Br J Pharmacol* **129**: 627-30 (2000)).

[0007] Moreover, patch clamp techniques have also been used to study the effect of the centrally acting muscle relaxant chlorzoxazone and three structurally related compounds, 1-ethyl-2-benzimidazolinone (1-EBIO), zoxazolamine, and 1,3-dihydro-1-[2-hydroxy-5-(trifluoromethyl)phenyl]-5-(trifluoromethyl)-2H-benzimidazol-2-one (NS 1619) on recombinant rat brain SK2 channels (rSK2 channels) expressed in HEK293 mammalian cells (Cao *et al.*, *J Pharmacol. Exp. Ther.* **296**: 683-689 (2001)). When applied externally, chlorzoxazone, 1-EBIO, and zoxazolamine activated rSK2 channel currents in cells dialyzed with a nominally calcium-free intracellular solution.

[0008] The effects of metal cations on the activation of recombinant human SK4 (also known as hIK1 or hKCa4) channels has also been studied (Cao and Houamed, *FEBS Lett.* **446**: 137-41 (1999)). The ion channels were expressed in HEK 293 cells and tested using patch clamp recording. Of the nine metals tested, cobalt, iron, magnesium, and zinc did not activate the SK4 channels when applied to the inside of SK4 channel-expressing membrane patches. Barium, cadmium, calcium, lead, and strontium activated SK4 channels in a

concentration-dependent manner. Calcium was the most potent metal, followed by lead, cadmium, strontium, and barium.

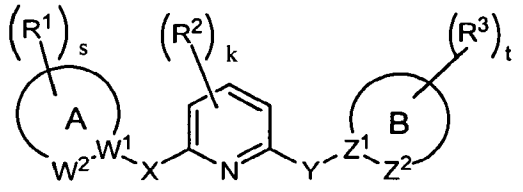
[0009] The SK channels are heteromeric complexes that comprise pore-forming α-subunits and the calcium binding protein calmodulin (CaM). CaM binds to the SK channel through the CaM-binding domain (CaMBD), which is located in an intracellular region of an α-subunit close to the pore. Based on a recently published crystal structure, calcium binding to the N-lobe of the CaM proteins on each of the four subunits initiates a structural change that allows a hydrophobic portion of the CaM protein to interact with a CaMBD on an adjacent subunit. As each N-lobe on an adjacent subunit grabs the other CaMBD C-terminal region, a rotary force is thought to be created between them which would drive open the channel.

[0010] New classes of compounds that act to block the opening of potassium ion channels would represent a significant advance in the art and provide the opportunity to develop treatment modalities for numerous diseases associated with these channels. The present invention provides a new class of potassium ion channel blocking compounds and methods of using the compounds.

BRIEF SUMMARY OF THE INVENTION

[0011] The present invention provides pyridinyl amines, prodrugs and pharmaceutically acceptable salts thereof ("compounds of the invention"), which are useful in the treatment of diseases through the modulation of potassium ion flow through potassium ion channels.

[0012] The compounds of the invention have a structure according to Formula I:



(I)

in which, A and B are independently selected from the group of substituted or unsubstituted 5- or 6- membered rings. The symbol W^1 is selected from $-C=$ and $-N-$. W^2 is selected from -CH=, -NH-, -N=, and -O-. The symbol Z^1 is selected from $-C=$, $-N-$, and $-\overset{\oplus}{N}=$. Z^2 is selected from -CH=, -NH-, -N=, and -O-. The symbol X is selected from a

bond, $-CH_2-$, and $-NR^4-$. Y is a bond, -CH=N-NH-, $-NH-CH_2-$, and $-NR^5-$. The symbols s, k, and t are integers independently selected from 1-5. R^1, R^2, R^3, and R^4 are members independently selected from H, OH, NH_2, NO_2, $-SO_2NH_2$, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted 3- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl. If the symbol s is greater than one, then each R^1 moiety can be the same or different than other R^1 moieties. If the symbol k is greater than one, then each R^2 moiety can be the same or different than other R^2 moieties. If the symbol t is greater than one, then each R^3 moiety can be the same or different than other R^3 moieties. Two R^1 groups (or two R^2 groups, or two R^3 groups, or R^1 and R^2, or R^2 and R^4, or R^2 and R^3, or R^1 and X, or R^2 and X, or R^2 and Y, or R^3 and Y) together with the atoms to which they are joined, optionally form a substituted or unsubstituted 5- to 7- membered ring.

[0013] In a second aspect, the present invention provides a method for decreasing ion flow through potassium ion channels in a cell, comprising contacting the cell with a potassium ion channel modulating amount of a compound according to Formula I.

[0014] In a third aspect, the present invention provides a method for treating a disease through the modulation of potassium ion flow through these channels. The compounds are useful in the treatment of central or peripheral nervous system disorders (*e.g.*, migraine, ataxia, Parkinson's disease, bipolar disorders, trigeminal neuralgia, spasticity, mood disorders, brain tumors, psychotic disorders, myokymia, seizures, epilepsy, hearing and vision loss, psychosis, anxiety, depression, dementia, memory and attention deficits, Alzheimer's disease, age-related memory loss, learning deficiencies, anxiety, traumatic brain injury, dysmenorrhea, narcolepsy and motor neuron diseases), and as neuroprotective agents (*e.g.*, to prevent stroke and the like). The compounds of the invention are also useful in treating disease states such as gastroesophogeal reflux disorder and gastrointestinal hypomotility disorders, irritable bowel syndrome, secretory diarrhea, asthma, cystic fibrosis, chronic obstructive pulmonary disease and rhinorrhea, convulsions, vascular spasms, coronary artery spasms, renal disorders, polycystic kidney disease, bladder spasms, urinary incontinence, bladder outflow obstruction, ischemia, cerebral ischemia, ischemic heart disease, angina pectoris, coronary heart disease, Reynaud's disease, intermittent claudication, Sjorgren's syndrome, arrhythmia, hypertension, myotonic muscle dystrophia, xerostomi, diabetes type II, hyperinsulinemia, premature labor, baldness, cancer, and immune

suppression. This method involves administering, to a patient, an effective amount of a compound having Formula I.

[0015] In a fourth aspect, the present invention provides a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to Formula I.

[0016] These and other aspects and embodiments of the invention will be apparent from the detailed description that follows.

DETAILED DESCRIPTION OF THE INVENTION

I. Abbreviations and Definitions

[0017] The abbreviations used herein have their conventional meaning within the chemical and biological arts.

[0018] Where substituent groups are specified by their conventional chemical formulae, written from left to right, they equally encompass the chemically identical substituents that would result from writing the structure from right to left, *e.g.*, $-CH_2O-$ is equivalent to $-OCH_2-$.

[0019] The term "alkyl," by itself or as part of another substituent, means, unless otherwise stated, a straight or branched chain, or cyclic hydrocarbon radical, or combination thereof, which may be fully saturated, mono- or polyunsaturated and can include di- and multivalent radicals, having the number of carbon atoms designated (*i.e.* C_1-C_{10} means one to ten carbons). Examples of saturated hydrocarbon radicals include, but are not limited to, groups such as methyl, ethyl, n-propyl, isopropyl, n-butyl, t-butyl, isobutyl, sec-butyl, cyclohexyl, (cyclohexyl)methyl, cyclopropylmethyl, homologs and isomers of, for example, n-pentyl, n-hexyl, n-heptyl, n-octyl, and the like. An unsaturated alkyl group is one having one or more double bonds or triple bonds. Examples of unsaturated alkyl groups include, but are not limited to, vinyl, 2-propenyl, crotyl, 2-isopentenyl, 2-(butadienyl), 2,4-pentadienyl, 3-(1,4-pentadienyl), ethynyl, 1- and 3-propynyl, 3-butynyl, and the higher homologs and isomers. The term "alkyl," unless otherwise noted, is also meant to include those derivatives of alkyl defined in more detail below, such as "heteroalkyl." Alkyl groups which are limited to hydrocarbon groups are termed "homoalkyl".

[0020] The term "alkylene" by itself or as part of another substituent means a divalent radical derived from an alkane, as exemplified, but not limited, by $-CH_2CH_2CH_2CH_2-$, and

further includes those groups described below as "heteroalkylene." Typically, an alkyl (or alkylene) group will have from 1 to 24 carbon atoms, with those groups having 10 or fewer carbon atoms being preferred in the present invention. A "lower alkyl" or "lower alkylene" is a shorter chain alkyl or alkylene group, generally having eight or fewer carbon atoms.

[0021] The terms "alkoxy," "alkylamino" and "alkylthio" (or thioalkoxy) are used in their conventional sense, and refer to those alkyl groups attached to the remainder of the molecule via an oxygen atom, an amino group, or a sulfur atom, respectively.

[0022] The term "heteroalkyl," by itself or in combination with another term, means, unless otherwise stated, a stable straight or branched chain, or cyclic hydrocarbon radical, or combinations thereof, consisting of the stated number of carbon atoms and at least one heteroatom selected from the group consisting of O, N, Si and S, and wherein the nitrogen and sulfur atoms may optionally be oxidized and the nitrogen heteroatom may optionally be quaternized. The heteroatom(s) O, N and S and Si may be placed at any interior position of the heteroalkyl group or at the position at which the alkyl group is attached to the remainder of the molecule. Examples include, but are not limited to, $-CH_2-CH_2-O-CH_3$, $-CH_2-C(=O)-CH_3$, $-CH_2-CH_2-CH_2-C(=O)-O-C(CH_3)-CH_3$, $-CH_2-CH_2-CH_2-C(=O)-N-CH(CH_3)$, $-CH_2-CH_2-CH_2-NH-CH_3$, $-CH_2-CH_2-N(CH_3)-CH_3$, $-CH_2-S-CH_2-CH_3$, $-CH_2-CH_2,-S(O)-CH_3$, $-CH_2-CH_2-S(O)_2-CH_3$, $-CH=CH-O-CH_3$, $-Si(CH_3)_3$, $-CH_2-CH=N-OCH_3$, and $-CH=CH-N(CH_3)-CH_3$. Up to two heteroatoms may be consecutive, such as, for example, $-CH_2-NH-OCH_3$ and $-CH_2-O-Si(CH_3)_3$. Similarly, the term "heteroalkylene" by itself or as part of another substituent means a divalent radical derived from heteroalkyl, as exemplified, but not limited by, $-CH_2-CH_2-S-CH_2-CH_2-$ and $-CH_2-S-CH_2-CH_2-NH-CH_2-$. For heteroalkylene groups, heteroatoms can also occupy either or both of the chain termini (*e.g.,* alkyleneoxy, alkylenedioxy, alkyleneamino, alkylenediamino, and the like). Still further, for alkylene and heteroalkylene linking groups, no orientation of the linking group is implied by the direction in which the formula of the linking group is written. For example, the formula $-C(O)_2R'-$ represents both $-C(O)_2R'-$ and $-R'C(O)_2-$.

[0023] The terms "cycloalkyl" and "heterocycloalkyl", by themselves or in combination with other terms, represent, unless otherwise stated, cyclic versions of "alkyl" and "heteroalkyl", respectively. Thus, a cycloalkyl or heterocycloalkyl include saturated and unsaturated ring linkages. Additionally, for heterocycloalkyl, a heteroatom can occupy the position at which the heterocycle is attached to the remainder of the molecule. Examples of

cycloalkyl include, but are not limited to, cyclopentyl, cyclohexyl, 1-cyclohexenyl, 3-cyclohexenyl, cycloheptyl, and the like. Examples of heterocycloalkyl include, but are not limited to, 1–(1,2,5,6-tetrahydropyridyl), 1-piperidinyl, 2-piperidinyl, 3-piperidinyl, 4-morpholinyl, 3-morpholinyl, tetrahydrofuran-2-yl, tetrahydrofuran-3-yl, tetrahydrothien-2-yl, tetrahydrothien-3-yl, 1–piperazinyl, 2-piperazinyl, and the like.

[0024] The terms "halo" or "halogen," by themselves or as part of another substituent, mean, unless otherwise stated, a fluorine, chlorine, bromine, or iodine atom. Additionally, terms such as "haloalkyl," are meant to include monohaloalkyl and polyhaloalkyl. For example, the term "halo(C_1-C_4)alkyl" is mean to include, but not be limited to, trifluoromethyl, 2,2,2-trifluoroethyl, 4-chlorobutyl, 3-bromopropyl, and the like.

[0025] The term "aryl" means, unless otherwise stated, a polyunsaturated, aromatic, hydrocarbon substituent which can be a single ring or multiple rings (preferably from 1 to 3 rings) which are fused together or linked covalently. The term "heteroaryl" refers to aryl groups (or rings) that contain from one to four heteroatoms selected from N, O, and S, wherein the nitrogen and sulfur atoms are optionally oxidized, and the nitrogen atom(s) are optionally quaternized. A heteroaryl group can be attached to the remainder of the molecule through a heteroatom. Non-limiting examples of aryl and heteroaryl groups include phenyl, 1-naphthyl, 2-naphthyl, 4-biphenyl, 1-pyrrolyl, 2-pyrrolyl, 3-pyrrolyl, 3-pyrazolyl, 2-imidazolyl, 4-imidazolyl, pyrazinyl, 2-oxazolyl, 4-oxazolyl, 2-phenyl-4-oxazolyl, 5-oxazolyl, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, 2-thiazolyl, 4-thiazolyl, 5-thiazolyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrimidyl, 4-pyrimidyl, 5-benzothiazolyl, purinyl, 2-benzimidazolyl, 5-indolyl, 1-isoquinolyl, 5-isoquinolyl, 2-quinoxalinyl, 5-quinoxalinyl, 3-quinolyl, and 6-quinolyl. Substituents for each of the above noted aryl and heteroaryl ring systems are selected from the group of acceptable substituents described below.

[0026] For brevity, the term "aryl" when used in combination with other terms (*e.g.*, aryloxy, arylthioxy, arylalkyl) includes both aryl and heteroaryl rings as defined above. Thus, the term "arylalkyl" is meant to include those radicals in which an aryl group is attached to an alkyl group (*e.g.*, benzyl, phenethyl, pyridylmethyl and the like) including those alkyl groups in which a carbon atom (*e.g.*, a methylene group) has been replaced by, for example, an oxygen atom (*e.g.*, phenoxymethyl, 2-pyridyloxymethyl, 3-(1-naphthyloxy)propyl, and the like).

[0027] The term "oxo" as used herein means an oxygen that is double bonded to a carbon atom.

[0028] Each of the above terms (*e.g.*, "alkyl," "heteroalkyl," "aryl" and "heteroaryl") are meant to include both substituted and unsubstituted forms of the indicated radical. Preferred substituents for each type of radical are provided below.

[0029] Substituents for the alkyl and heteroalkyl radicals (including those groups often referred to as alkylene, alkenyl, heteroalkylene, heteroalkenyl, alkynyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, and heterocycloalkenyl) can be one or more of a variety of groups selected from, but not limited to: -OR', =O, =NR', =N-OR', -NR'R", -SR', -halogen, -SiR'R"R"', -OC(O)R', -C(O)R', $-CO_2R'$, -CONR'R", -OC(O)NR'R", -NR"C(O)R', -NR'-C(O)NR"R"', $-NR"C(O)_2R'$, -NR-C(NR'R"R"')=NR"", -NR-C(NR'R")=NR"', $-S(O)_2R'$, $-S(O)_2NR'R"$, $-NRSO_2R'$, -CN and $-NO_2$ in a number ranging from zero to (2m'+1), where m' is the total number of carbon atoms in such radical. R', R", R"' and R"" each preferably independently refer to hydrogen, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, *e.g.*, aryl substituted with 1-3 halogens, substituted or unsubstituted alkyl, alkoxy or thioalkoxy groups, or arylalkyl groups. When a compound of the invention includes more than one R group, for example, each of the R groups is independently selected as are each R', R", R"' and R"" groups when more than one of these groups is present. When R' and R" are attached to the same nitrogen atom, they can be combined with the nitrogen atom to form a 5-, 6-, or 7-membered ring. For example, -NR'R" is meant to include, but not be limited to, 1-pyrrolidinyl and 4-morpholinyl. From the above discussion of substituents, one of skill in the art will understand that the term "alkyl" is meant to include groups including carbon atoms bound to groups other than hydrogen groups, such as haloalkyl (*e.g.*, $-CF_3$ and $-CH_2CF_3$) and acyl (*e.g.*, $-C(O)CH_3$, $-C(O)CF_3$, $-C(O)CH_2OCH_3$, and the like).

[0030] Similar to the substituents described for the alkyl radical, substituents for the aryl and heteroaryl groups are varied and are selected from, for example: halogen, -OR', =O, =NR', =N-OR', -NR'R", -SR', -halogen, -SiR'R"R"', -OC(O)R', -C(O)R', $-CO_2R'$, -CONR'R", -OC(O)NR'R", -NR"C(O)R', -NR'-C(O)NR"R"', $-NR"C(O)_2R'$, -NR-C(NR'R"R"')=NR"", -NR-C(NR'R")=NR"', $-S(O)_2R'$, $-S(O)_2NR'R"$, $-NRSO_2R'$, -CN and $-NO_2$, -R', $-N_3$, $-CH(Ph)_2$, fluoro(C_1-C_4)alkoxy, and fluoro(C_1-C_4)alkyl, in a number ranging from zero to the total number of open valences on the aromatic ring

system; and where R', R", R"' and R"" are preferably independently selected from hydrogen, alkyl, heteroalkyl, aryl and heteroaryl. When a compound of the invention includes more than one R group, for example, each of the R groups is independently selected as are each R', R", R"' and R"" groups when more than one of these groups is present.

[0031] Two of the substituents on adjacent atoms of the aryl or heteroaryl ring may optionally be replaced with a substituent of the formula $-T-C(O)-(CRR')_q-U-$, wherein T and U are independently –NR-, -O-, -CRR'- or a single bond, and q is an integer of from 0 to 3. Alternatively, two of the substituents on adjacent atoms of the aryl or heteroaryl ring may optionally be replaced with a substituent of the formula $-A-(CH_2)_r-B-$, wherein A and B are independently –CRR'-, -O-, -NR-, -S-, -S(O)-, $-S(O)_2-$, $-S(O)_2NR'-$ or a single bond, and r is an integer of from 1 to 4. One of the single bonds of the new ring so formed may optionally be replaced with a double bond. Alternatively, two of the substituents on adjacent atoms of the aryl or heteroaryl ring may optionally be replaced with a substituent of the formula $-(CRR')_s-X-(CR"R"')_d-$, where s and d are independently integers of from 0 to 3, and X is -O-, -NR'-, -S-, -S(O)-, $-S(O)_2-$, or $-S(O)_2NR'-$. The substituents R, R', R" and R"' are preferably independently selected from hydrogen or substituted or unsubstituted (C_1-C_6)alkyl.

[0032] As used herein, the term "heteroatom" is meant to include oxygen (O), nitrogen (N), sulfur (S) and silicon (Si).

[0033] The term "pharmaceutically acceptable salts" is meant to include salts of the active compounds which are prepared with relatively nontoxic acids or bases, depending on the particular substituents found on the compounds described herein. When compounds of the present invention contain relatively acidic functionalities, base addition salts can be obtained by contacting the neutral form of such compounds with a sufficient amount of the desired base, either neat or in a suitable inert solvent. Examples of pharmaceutically acceptable base addition salts include sodium, potassium, calcium, ammonium, organic amino, or magnesium salt, or a similar salt. When compounds of the present invention contain relatively basic functionalities, acid addition salts can be obtained by contacting the neutral form of such compounds with a sufficient amount of the desired acid, either neat or in a suitable inert solvent. Examples of pharmaceutically acceptable acid addition salts include those derived from inorganic acids like hydrochloric, hydrobromic, nitric, carbonic, monohydrogencarbonic, phosphoric, monohydrogenphosphoric, dihydrogenphosphoric, sulfuric, monohydrogensulfuric, hydriodic, or phosphorous acids and the like, as well as the

salts derived from relatively nontoxic organic acids like acetic, propionic, isobutyric, maleic, malonic, benzoic, succinic, suberic, fumaric, lactic, mandelic, phthalic, benzenesulfonic, p-tolylsulfonic, citric, tartaric, methanesulfonic, and the like. Also included are salts of amino acids such as arginate and the like, and salts of organic acids like glucuronic or galactunoric acids and the like (*see*, for example, Berge *et al.*, "Pharmaceutical Salts", *Journal of Pharmaceutical Science* 66: 1-19 (1977)). Certain specific compounds of the present invention contain both basic and acidic functionalities that allow the compounds to be converted into either base or acid addition salts.

[0034] The neutral forms of the compounds are preferably regenerated by contacting the salt with a base or acid and isolating the parent compound in the conventional manner. The parent form of the compound differs from the various salt forms in certain physical properties, such as solubility in polar solvents.

[0035] In addition to salt forms, the present invention provides compounds, which are in a prodrug form. Prodrugs of the compounds described herein are those compounds that readily undergo chemical changes under physiological conditions to provide the compounds of the present invention. Additionally, prodrugs can be converted to the compounds of the present invention by chemical or biochemical methods in an *ex vivo* environment. For example, prodrugs can be slowly converted to the compounds of the present invention when placed in a transdermal patch reservoir with a suitable enzyme or chemical reagent.

[0036] The term "ring" as used herein means an encircling arrangement of atoms optionally having heteroatoms within the arrangement. A ring includes aromatic and non-aromatic moieties such as substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl. The number of atoms in a ring are typically defined by the number of members in the ring. For example, a "5- to 7- membered ring" means there are 5-7 atoms in the encircling arrangement. Each member is optionally a heteroatom. Thus, the term "5- to 7- membered ring" includes, for example pyridinyl, piperidinyl and thiazolyl rings. Rings are typically drawn with a single explicit substituent within parentheses having a subscript letter. The subscript letter typically represents a set of integers, such as 1-10. The integers represent the number of ring substituents wherein each substituent is optionally different. For example, for the substituent $(R^1)_s$, where s is 2, the ring may be substituted with each a substituted or unsubstituted alkyl and a substituted or unsubstituted heteroalkyl.

[0037] The term "poly" as used herein means at least 2. For example, a polyvalent metal ion is a metal ion having a valency of at least 2.

[0038] "Moiety" refers to the radical of a molecule that is attached to another moiety.

[0039] The symbol ∿∿∿, whether utilized as a bond or displayed perpendicular to a bond indicates the point at which the displayed moiety is attached to the remainder of the molecule.

[0040] Certain compounds of the present invention can exist in unsolvated forms as well as solvated forms, including hydrated forms. In general, the solvated forms are equivalent to unsolvated forms and are encompassed within the scope of the present invention. Certain compounds of the present invention may exist in multiple crystalline or amorphous forms. In general, all physical forms are equivalent for the uses contemplated by the present invention and are intended to be within the scope of the present invention.

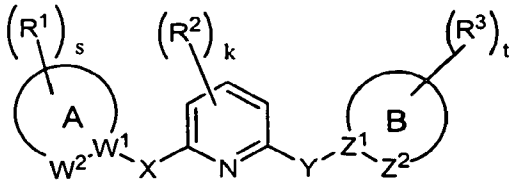
[0041] Certain compounds of the present invention possess asymmetric carbon atoms (optical centers) or double bonds; the racemates, diastereomers, geometric isomers and individual isomers are encompassed within the scope of the present invention.

[0042] The compounds of the present invention may also contain unnatural proportions of atomic isotopes at one or more of the atoms that constitute such compounds. For example, the compounds may be radiolabeled with radioactive isotopes, such as for example tritium (^{3}H), iodine-125 (^{125}I) or carbon-14 (^{14}C). All isotopic variations of the compounds of the present invention, whether radioactive or not, are encompassed within the scope of the present invention.

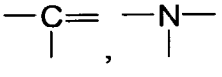
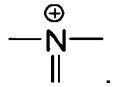
II. Potassium Ion Channel Modulators

[0043] The invention provides potassium ion channel modulators that include a pyridinyl moiety and a first and a second ring, each of said rings being attached, either directly or through a linker, to the pyridinyl moiety.

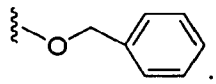
[0044] The compounds of the invention have a structure according to Formula I:



(I)

in which, A and B are independently selected from the group of substituted or unsubstituted 5- or 6- membered rings. The symbol W^1 is selected from  and  . W^2 is selected from -CH=, -NH-, -N=, and -O-. The symbol Z^1 is selected from  , and  . Z^2 is selected from -CH=, -NH-, -N=, and -O-. The symbol X is selected from a bond, $-CH_2-$, and $-NR^4-$. Y is a bond, -CH=N-NH-, $-NH-CH_2-$, and $-NR^5-$. The symbols s, k, and t are integers independently selected from 1-5. R^1, R^2, R^3, and R^4 are members independently selected from H, OH, NH_2, NO_2, $-SO_2NH_2$, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted 3- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl. If the symbol s is greater than one, then each R^1 moiety can be the same or different than other R^1 moieties. If the symbol k is greater than one, then each R^2 moiety can be the same or different than other R^2 moieties. If the symbol t is greater than one, then each R^3 moiety can be the same or different than other R^3 moieties. Two R^1 groups (or two R^2 groups, or two R^3 groups, or R^1 and R^2, or R^2 and R^4, or R^2 and R^3, or R^1 and X, or R^2 and X, or R^2 and Y, or R^3 and Y) together with the atoms to which they are joined, optionally form a substituted or unsubstituted 5- to 7- membered ring.

[0045] In an exemplary embodiment, R^1 is selected from H, OH, NH_2, NO_2, halogen, substituted or unsubstituted (C_1-C_5) alkyl, substituted or unsubstituted 1- to 5- membered heteroalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl. In another exemplary embodiment, R^1 is selected from H, NH_2, Br, F, Cl, CF_3, methyl, $-OCH_3$, -NH-C(O)-CH_3, -NH-C(O)-CH_2CH_3 and morpholinyl.

[0046] In an exemplary embodiment, R^2 is selected from H, Cl, F, OH, NH_2, substituted or unsubstituted alkyl, and substituted or unsubstituted heteroalkyl. In another exemplary embodiment, R^2 is selected from H, OH, NH_2, substituted or unsubstituted (C_1-C_6) alkyl, and substituted or unsubstituted 1- to 6- membered heteroalkyl. In yet another exemplary embodiment, R^2 is selected from H, OH, NH_2, methyl, CF_3, $-OCH_3$, $-OCH(CH_3)_2$, $-OCH_2CH_2OCH_3$, $-OCH_2C(O)OCH_3$, CN, $-NHC(O)CH_3$, $-C(O)OCH_3$, $C(O)N(CH_3)_2$, and  .

[0047] In an exemplary embodiment, R^3 is selected from H, OH, NH_2, NO_2, $-SO_2NH_2$, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted (C_5-C_7) cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl.

[0048] In another exemplary embodiment, R^3 is selected from H, NH_2, NO_2, $-SO_2NH_2$, $-L^1OR^8$, $-L^2NR^9R^{10}$, $-L^3C(O)NR^{11}R^{12}$, $-L^4C(O)OR^{13}$, $-L^5C(O)R^{14}$, Cl, F, I, Br, substituted or unsubstituted (C_1-C_7) alkyl, substituted or unsubstituted morpholinyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted pyrrolidinonyl, substituted or unsubstituted pyridinyl, substituted or unsubstituted phenyl, substituted or unsubstituted piperidinyl, substituted or unsubstituted piperazinyl, substituted or unsubstituted thiophenyl, substituted or unsubstituted pyrrolidinyl, and substituted or unsubstituted furanyl. In an exemplary embodiment, R^8 is selected from H, substituted or unsubstituted (C_1-C_6) alkyl, substituted or unsubstituted 1- to 6- membered heteroalkyl, substituted or unsubstituted 5- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted aryl. R^9 and R^{10} are members independently selected from H, substituted or unsubstituted (C_1-C_6) alkyl, substituted or unsubstituted 1- to 6- membered heteroalkyl, and substituted or unsubstituted heteroaryl. R^9 and R^{10}, together with the nitrogen to which they are joined, optionally form a 5- to 7- membered ring. R^{11} and R^{12} are members independently selected from H, substituted or unsubstituted (C_1-C_6) alkyl, substituted or unsubstituted 1- to 6- membered heteroalkyl, and substituted or unsubstituted heteroaryl. R^{11} and R^{12} together with the nitrogen to which they are joined optionally form a 5- to 7- membered ring. R^{13} is selected from H, substituted or unsubstituted (C_1-C_6) alkyl, substituted or unsubstituted 1- to 6- membered heteroalkyl, substituted or unsubstituted 5- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted aryl. R^{14} is selected from H, substituted or unsubstituted (C_1-C_6) alkyl, substituted or unsubstituted 1- to 6- membered heteroalkyl, substituted or unsubstituted 5- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted aryl. L^1, L^2, L^3, L^4 and L^5 are members independently selected from a bond, -NH-, and substituted or unsubstituted (C_1-C_6) alkylene.

[0049] In another exemplary embodiment, R^8 is selected from H, methyl, $-CH_2CH_2N(CH_3)_2$, and benzyl. R^9 and R^{10} are members independently selected from H, methyl, $-C(O)CH_3$ and pyridinyl. R^9 and R^{10} together with the nitrogen to which they are joined optionally form an unsubstituted pyrrolidine ring. R^{11} and R^{12} are members independently selected from H and ethyl. R^{13} is selected from H, methyl and ethyl. R^{14} is selected from H and methyl. L^1 is selected from a bond, methylene, ethylene, and propylene. L^2 is selected from a bond, methylene, and ethylene. L^3 is a bond. L^4 is selected from a bond and ethylene. L^5 is a bond. Unsubstituted (C_1-C_7) alkyl is selected from methyl, ethyl, hexyl, isopropyl, isopropenyl, and isobutyl. Substituted (C_1-C_7) alkyl is CF_3. Substituted pyridinyl is substituted with at least one pyridinyl substituent, wherein said pyridinyl substituent is selected from methyl, I, Cl, F, $-OCH_2CH_3$ and unsubstituted thiazolyl. Substituted phenyl is substituted with at least one phenyl substituent, wherein said phenyl substituent is selected from F, $-N(CH_3)_2$ and $-OCH_3$. Substituted piperidinyl, substituted piperazinyl and substituted furanyl are each substituted with a methyl.

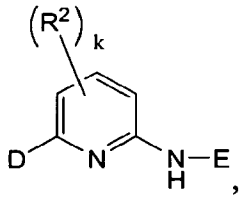
[0050] In an exemplary embodiment, R^4 and R^5 are members independently selected from H, substituted or unsubstituted alkyl, and substituted or unsubstituted heteroalkyl. In another exemplary embodiment, R^4 and R^5 are members independently selected from H, substituted or unsubstituted (C_1-C_6) alkyl, substituted or unsubstituted 1- to 6- membered heteroalkyl, and substituted or unsubstituted 5- to 7- membered heteroaryl. In yet another exemplary embodiment, R^4 and R^5 are members independently selected from H, methyl, $-C(O)OC(CH_3)_3$, $-C(O)CH_3$, and pyridinyl.

[0051] In an exemplary embodiment, A is selected from substituted or unsubstituted thiophenyl, substituted or unsubstituted benzyl, substituted or unsubstituted pyridinyl, substituted or unsubstituted pyrimidinyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted pyrazinyl, substituted or unsubstituted pyrazolyl, and substituted or unsubstituted 1,2,4-oxadiazolyl. B is selected from substituted or unsubstituted furanyl, substituted or unsubstituted benzyl, substituted or unsubstituted pyridinyl, substituted or unsubstituted 1,2,4-thiadiazole, substituted or unsubstituted pyrimidinyl, substituted or unsubstituted pyrazinyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted isoxazolyl, and substituted or unsubstituted pyrazolyl.

[0052] In an exemplary embodiment, the compounds of the invention also comprise a polyvalent metal ion and a polydentate component of a metal ion chelator, where said polydentate component has a structure according to Formula I.

[0053] In an exemplary embodiment, two R^3 groups together with the atoms to which they are joined optionally form a substituted or unsubstituted phenyl or substituted or unsubstituted cyclohexanyl. R^1 and R^2 together with the atoms to which they are joined optionally form a substituted or unsubstituted phenyl or substituted or unsubstituted cyclohexanyl. R^2 and R^5 together with the atoms to which they are joined optionally form a substituted or unsubstituted imidazolyl or substituted or unsubstituted morpholinyl.

[0054] In an exemplary embodiment, there is a compound of the structure



in which k is a whole number between 1 and 3. D is selected from substituted or unsubstituted 2-pyridinyl, substituted or unsubstituted 2-pyrimidinyl, substituted or unsubstituted 2-thiazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted 1-pyrazolyl, substituted or unsubstituted 2-pyrazinyl. E is selected from substituted or unsubstituted 2-pyridinyl, substituted or unsubstituted 3-pyrazolyl, substituted or unsubstituted 2-thiadiazolyl, substituted or unsubstituted 3-isoxazolyl. R^2 is selected from H, OH, NH_2, NO_2, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted 3- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl.

[0055] In a second aspect, the present invention provides a method for decreasing ion flow through potassium ion channels in a cell, comprising contacting the cell with a potassium ion channel modulating amount of a compound according to Formula I.

[0056] In an exemplary embodiment, the potassium ion channel comprises at least one SK subunit.

[0057] In a third aspect, the present invention provides a method for treating a disease through the modulation of potassium ion flow through these channels. The compounds are

useful in the treatment of central or peripheral nervous system disorders (*e.g.*, migraine, ataxia, Parkinson's disease, bipolar disorders, trigeminal neuralgia, spasticity, mood disorders, brain tumors, psychotic disorders, myokymia, seizures, epilepsy, hearing and vision loss, psychosis, anxiety, depression, dementia, memory and attention deficits, Alzheimer's disease, age-related memory loss, learning deficiencies, anxiety, traumatic brain injury, dysmenorrhea, narcolepsy and motor neuron diseases), and as neuroprotective agents (*e.g.*, to prevent stroke and the like). The compounds of the invention are also useful in treating disease states such as gastroesophogeal reflux disorder and gastrointestinal hypomotility disorders, irritable bowel syndrome, secretory diarrhea, asthma, cystic fibrosis, chronic obstructive pulmonary disease and rhinorrhea, convulsions, vascular spasms, coronary artery spasms, renal disorders, polycystic kidney disease, bladder spasms, urinary incontinence, bladder outflow obstruction, ischemia, cerebral ischemia, ischemic heart disease, angina pectoris, coronary heart disease, Reynaud's disease, intermittent claudication, Sjorgren's syndrome, arrhythmia, hypertension, myotonic muscle dystrophia, xerostomi, diabetes type II, hyperinsulinemia, premature labor, baldness, cancer, and immune suppression. This method involves administering, to a patient, an effective amount of a compound having Formula I.

[0058] In a fourth aspect, the present invention provides a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to Formula I.

Preparation of Potassium Ion Channel Modulators

[0059] The following exemplary schemes illustrate methods of preparing the compounds of the invention. These methods are not limited to producing the compounds shown, but can be used to prepare other compounds of Formula I as well. The compounds of the invention can also be produced by methods not explicitly illustrated in the schemes but are well within the skill of one in the art. The compounds can be prepared using readily available starting materials or known intermediates.

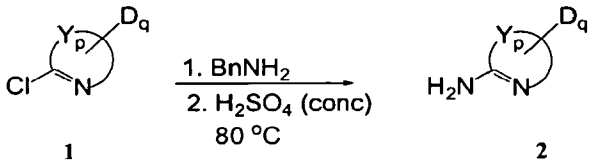
[0060] In the following schemes, the symbol Y is independently selected from $(CH_2)_n$, N, S, and O. The symbol D is independently selected from H, OH, NH_2, NO_2, $-SO_2NH_2$, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted 3- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted aryl, and substituted or

unsubstituted heteroaryl. The symbol p is independently selected from 0-5. The symbol q is independently selected from 0-5.

[0061] The substituents of the pyridinyl compounds of the invention can be produced through the methods outlined in Schemes 1-8.

[0062] In one embodiment, the substituents of the invention comprise amino-substituted heteroaryl moieties as shown in Schemes 1-6.

Scheme 1

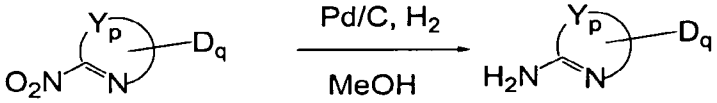


1 2

[0063] In Scheme 1, compound **1** is reacted with benzylamine, followed by debenzylation in concentrated sulfuric acid to produce **2**.

[0064] An alternative route to producing compound **2** is shown in Scheme 2.

Scheme 2

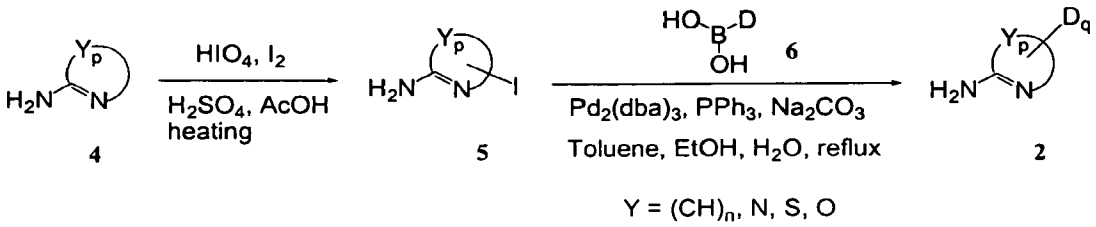


3 2

[0065] In Scheme 2, a compound **3** is reduced to form compound **2**.

[0066] Substituents can be added to the amino-substituted heteroaryl moieties as described in Schemes 3-6.

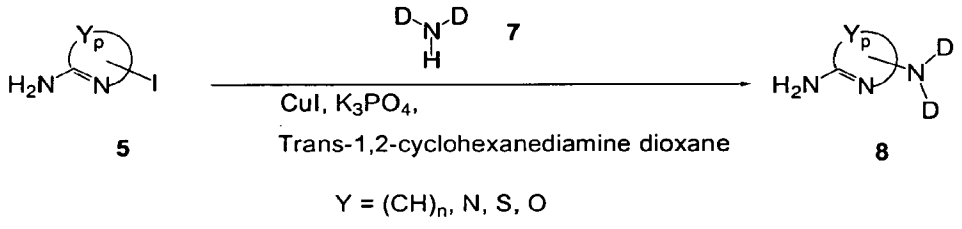
Scheme 3



[0067] In Scheme 3, compound **4** is iodinated to produce a halosubstituted 2-amino-aza-heterocycle **5**. This compound is reacted with a boronic acid **6** in the presence of tris(dibenzylideneacetone)dipalladium(0) ($Pd_2(dba)_3$), and PPh_3 in toluene, ethanol, and water to produce **2**.

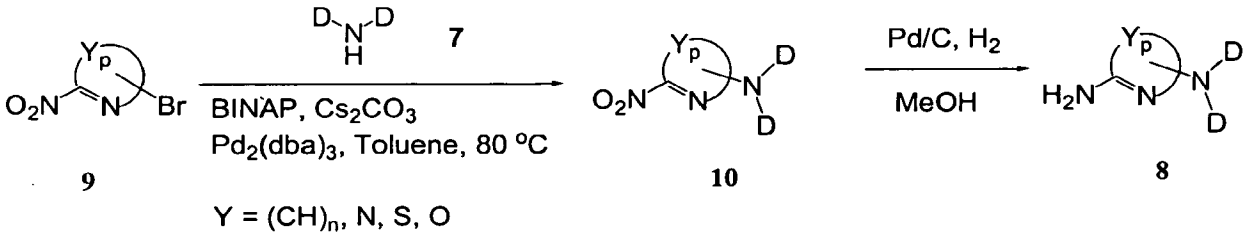
[0068] In another example, amino substituents can be added to the heteroaryl moieties in the following manner.

Scheme 4



[0069] In Scheme 4, an iodo-substituted 2-amino-aza-heterocycle **5** is reacted with an amine **7** or amide using copper catalyzed coupling chemistry to generate a 2-amino-aza-heterocycle **8**.

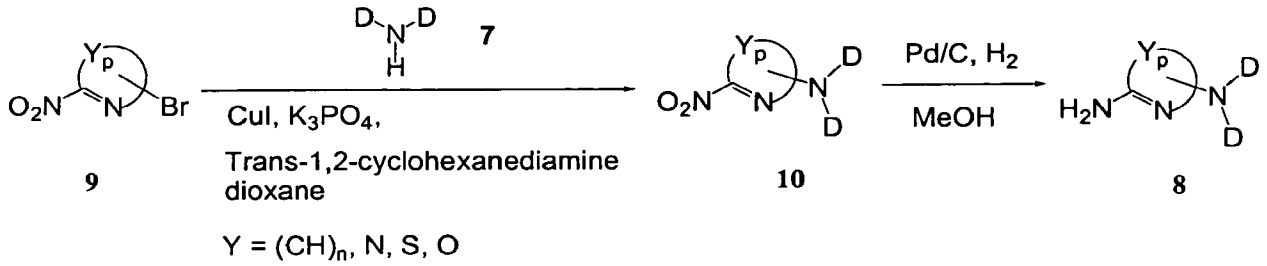
Scheme 5



[0070] In Scheme 5, a bromo-substituted 2-nitro-aza-heterocycle **9** is reacted with an amine **7** or amide using palladium-catalyzed coupling chemistry to generate an aminosubstituted 2-

nitro-aza-heterocycle **10**. The nitro adduct is reduced to an amino adduct **8** by a palladium catalyzed hydrogenation.

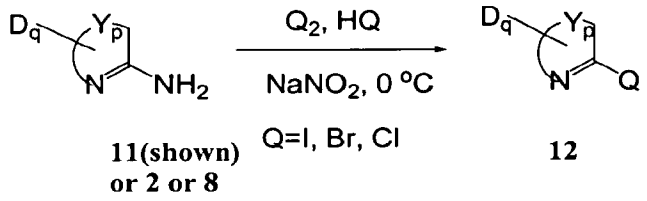
Scheme 6



[0071] In Scheme 6, a bromo-substituted 2-nitro-aza-heterocycle **9** is reacted with an amine **7** or amide using copper catalyzed coupling chemistry to generate an aminosubstituted 2-nitro-aza-heterocycle **10**. The nitro adduct is reduced to an amino adduct **8** by a palladium catalyzed hydrogenation.

[0072] In one embodiment, the substituents of the invention comprise halo-substituted heteroaryl moieties as shown in Scheme 7.

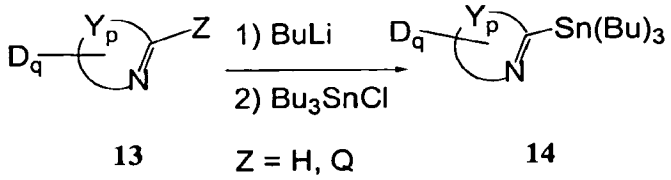
Scheme 7



[0073] In Scheme 7, compound **11** or **2** or **8** is halogenated by diazotization followed by sodium nitrite in the presence of acid containing halogen at 0°C to produce compound **12**.

[0074] In another embodiment, the substituents of the invention comprise stannyl-substituted heteroaryl moieties as shown in Scheme 8.

Scheme 8

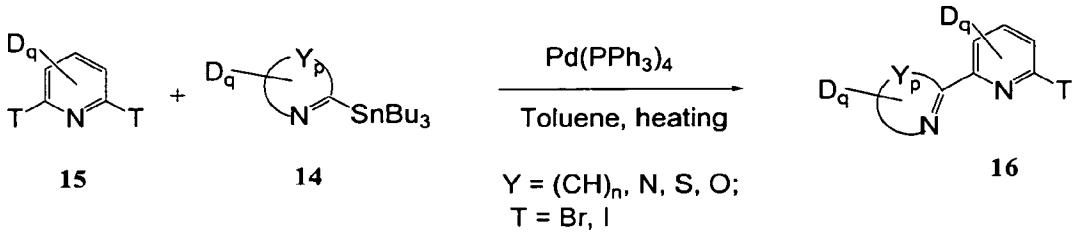


[0075] In Scheme 8, compound **13** is stannylated with *n*-butyllithium to produce compound **14**.

[0076] A first substituent of the pyridinyl compound can be attached through the methods outlined in Scheme 9 or Scheme 10.

[0077] In one embodiment, stannyl-substituted heteroaryl moieties can be attached to the pyridinyl core as shown in Scheme 9.

Scheme 9

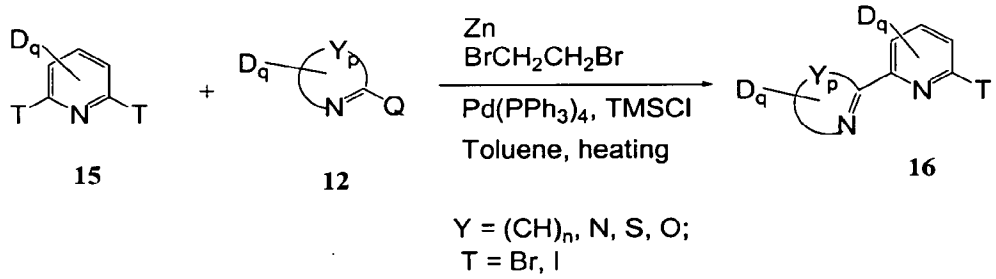


15 **14** **16**

[0078] In Scheme 9, addition of compound **14** to a 2,6-dihalopyridine **15** in the presence of a palladium catalyst in toluene produces compound **16**.

[0079] In another embodiment, halo-substituted heteroaryl moieties can be attached to the pyridinyl core as shown in Scheme 10.

Scheme 10

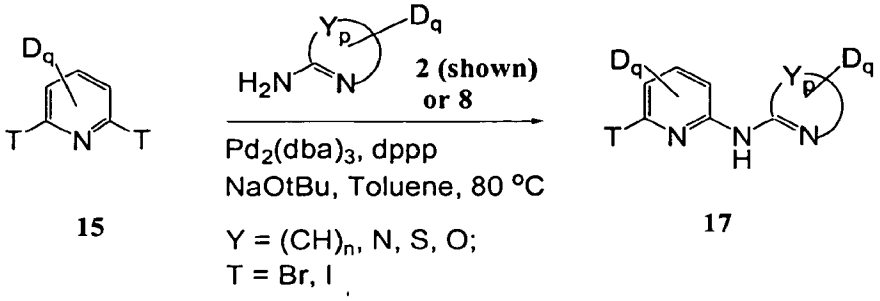


15 **12** **16**

[0080] In Scheme 10, addition of compound **12** to a 2,6-dihalopyridine **15** in the presence of zinc dust, dibromoethane, and a palladium catalyst in toluene produces compound **16**.

[0081] In another embodiment, amino-substituted heteroaryl moieties can be attached to the pyridinyl core as shown in Scheme 11.

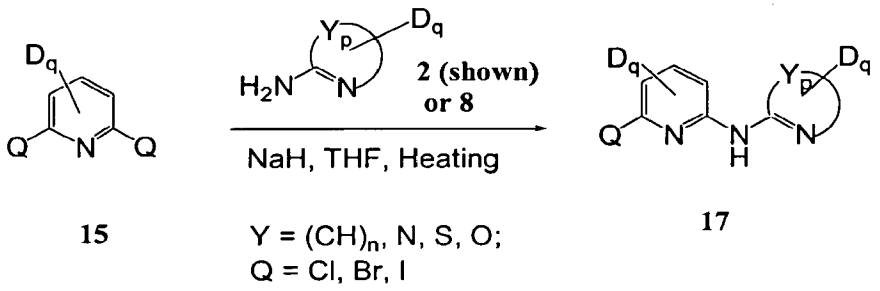
Scheme 11



[0082] In Scheme 11, addition of compound **2** or **8** to a 2,6-dihalopyridine **15** in the presence of a palladium catalyst in toluene with 1,3-bis(diphenyl phosphino)propane (dppp) produces compound **17**.

[0083] An alternative method of attaching a first substituent is illustrated in Scheme 12:

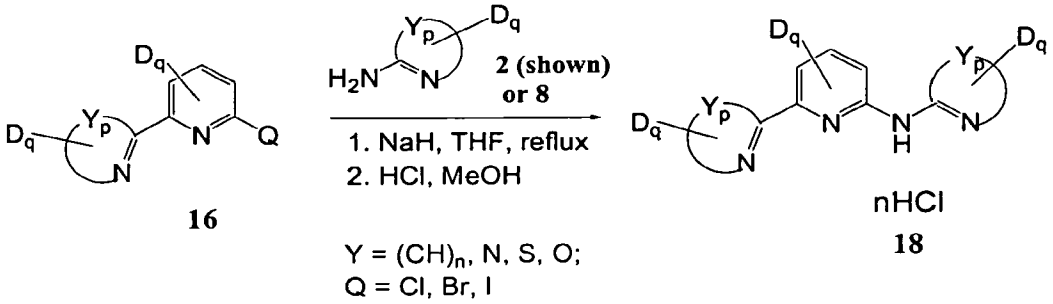
Scheme 12



[0084] In Scheme 12, addition of compound **2** or **8** to a 2,6-dihalopyridine **15** via sodium hydride in tetrahydrofuran (THF) produces compound **17**.

[0085] Bis-substituted pyridines are produced from the methods outlined in Scheme 13 or Scheme 14 or Scheme 15.

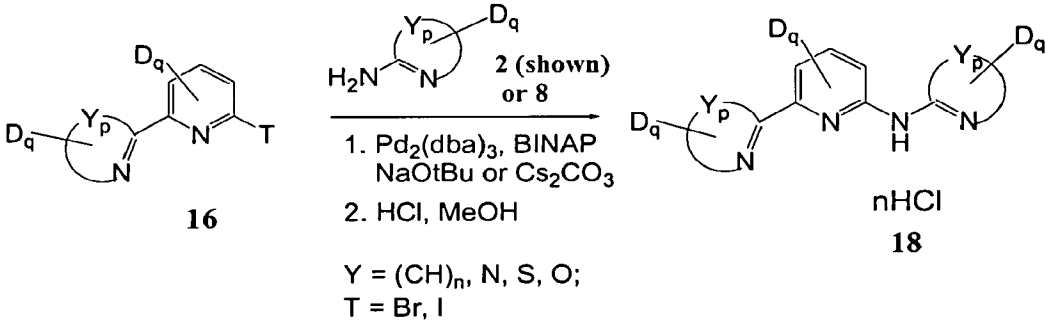
Scheme 13



[0086] In Scheme 13, compound **2** or **8** is mixed with sodium hydride to facilitate the nucleophilic addition of **2** or **8** to compound **16**. A final acid washing step produces a bis-substituted pyridine **18**.

[0087] Alternative conditions for facilitating this transformation are provided in Scheme 14.

Scheme 14

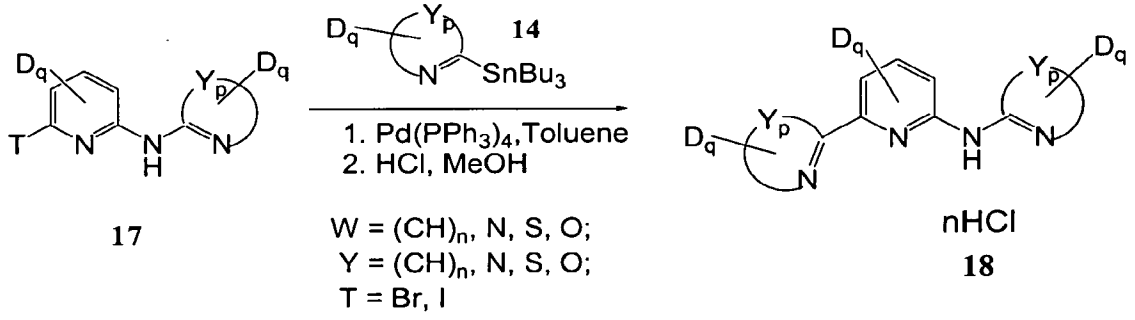


16 **18**

[0088] In Scheme 14, addition of compound **2** or **8** to compound **16** in the presence of a palladium catalyst produces compound **18**. A final acid washing step produces a bis-substituted pyridine **18**.

[0089] Compound **18** is alternatively produced as shown in Scheme 15.

Scheme 15

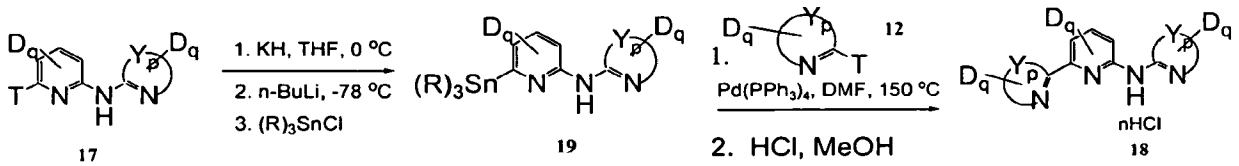


17 **18**

[0090] In Scheme 15, compound **14** is added to compound **17** in the presence of a palladium catalyst to form compound **18**. A final acid washing step produces a bis-substituted pyridine **18**.

[0091] An alternative method of creating substituted pyridine compounds is illustrated in Scheme 16:

Scheme 16



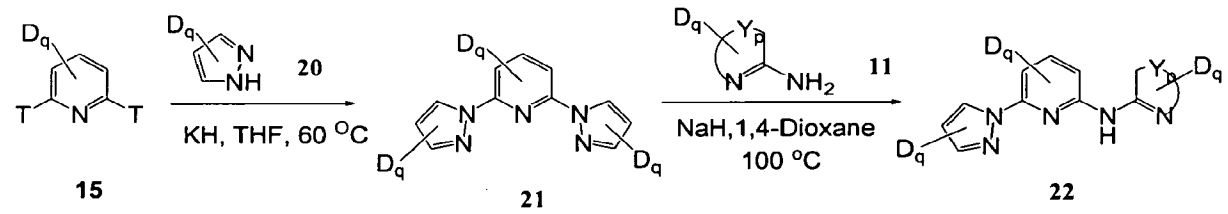
17 19 12 18

Y = $(CH)_n$, N, S, O; T= I, Br

[0092] In Scheme 16, compound **17** is first stannylated to produce compound **19**. Next, compound **12** is added in the presence of a palladium catalyst to produce the final product **18**. A final acid washing step produces a bis-substituted pyridine **18**.

[0093] Another method of producing the compounds of the invention is exemplified in Scheme 17:

Scheme 17

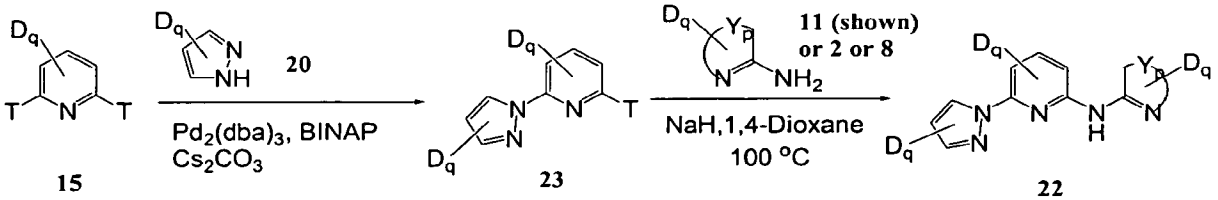


15 21 22

T = I, Br; Y = $(CH)_n$, N, S, O

[0094] In Scheme 17, compound **15** is mixed with potassium hydride in THF to facilitate the nucleophilic addition of an excess of pyrazole **20** to compound **15** to produce a bis-pyrazoyl pyridine **21**. Sodium hydride is then mixed with compound **11** to facilitate the production of compound **22**.

Scheme 18



15 23 22

T = I, Br; Y = $(CH)_n$, N, S, O

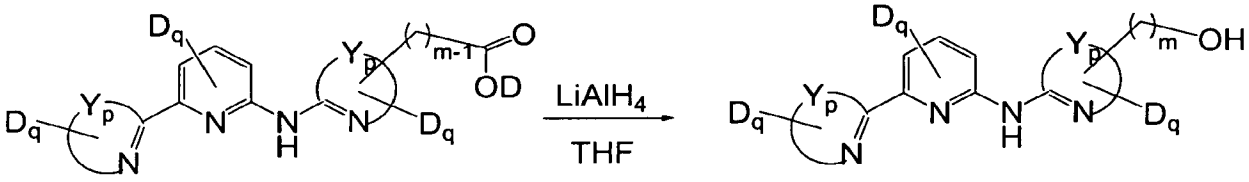
[0095] In Scheme 18, 1 equivalent of compound **20** is coupled to compound **15** via palladium catalyzed coupling chemistry to produce mono-pyrazolyl pyridine **23**. Sodium

hydride is then mixed with compound **11** or **2** or **8** to facilitate its addition to compound **23** and the production of compound **22**.

[0096] Methods of modifying the pyridinyl compounds of the invention are described in Scheme 19-23.

[0097] A method of creating a pyridinyl compounds of the invention with an alcohol substituent is outlined in Scheme 19.

Scheme 19

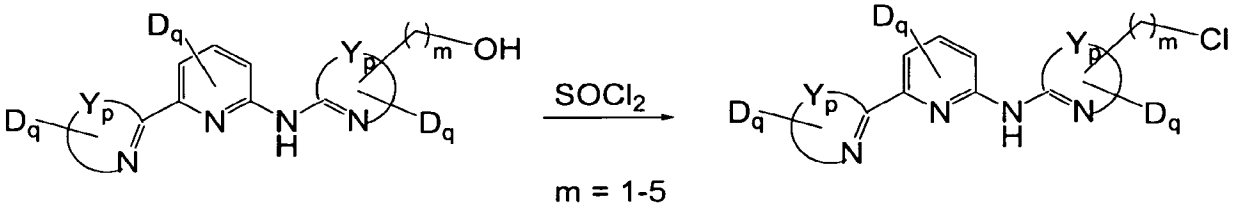


18 **24**

[0098] In Scheme 19, compound **18** is reduced to compound **24** through the use of $LiAlH_4$ in THF.

[0099] A method of chlorinating the pyridinyl compounds of the invention is outlined in Scheme 20.

Scheme 20

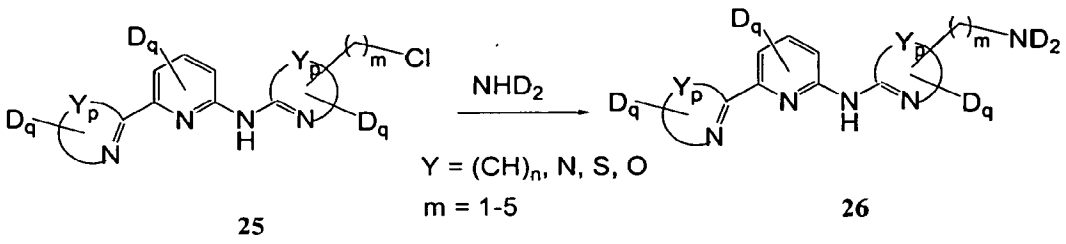


24 **25**

[0100] In Scheme 20, compound **24** is converted to compound **25** through the use of $SOCl_2$.

[0101] A method of adding an amine to the pyridinyl compounds of the invention is outlined in Scheme 21.

Scheme 21

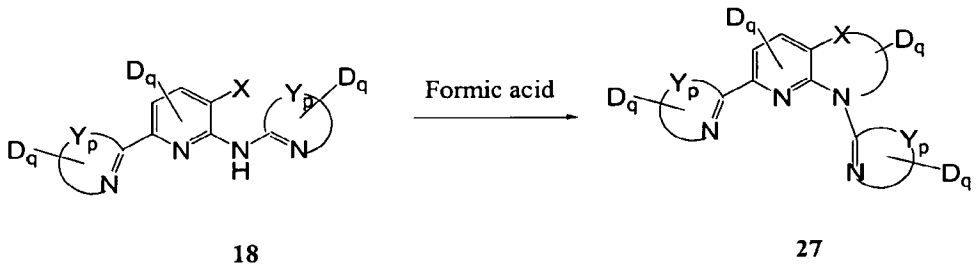


25 26

[0102] In Scheme 21, compound **25** is reacted with any commercially available primary or secondary amine in order to produce compound **26**.

[0103] A method of creating a bicyclic pyridinyl compound of the invention is outlined in Scheme 22.

Scheme 22



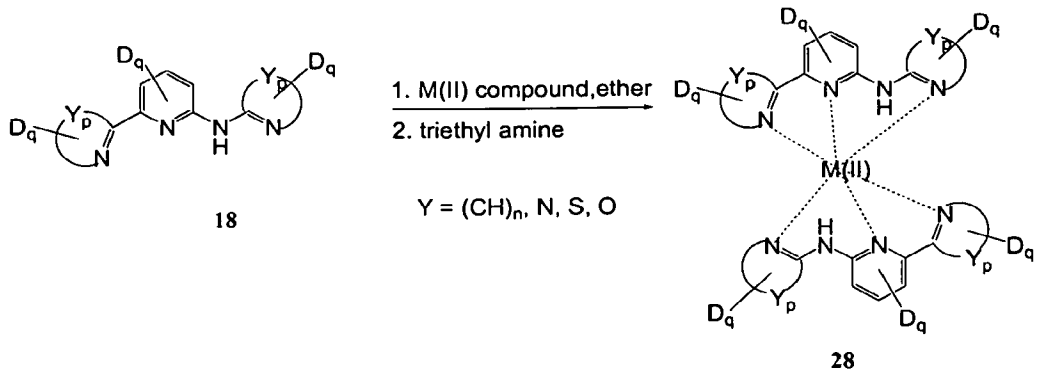
18 27

[0104] In Scheme 22, compound **18** is reacted with formic acid to produce compound **27**.

[0105] The compounds of the invention also include metal complexes. These metal complexes comprise a polyvalent metal ion and a pyridinyl compound of the invention. In an exemplary embodiment, the polyvalent metal ion can be a transition metal. In another exemplary embodiment, the polyvalent metal ion is a member selected from iron, zinc, copper, cobalt, manganese, and nickel.

[0106] A method of creating metal-pyridinyl complexes of the invention is outlined in Scheme 23.

Scheme 23



18

28

[0107] In Scheme 23, compound **18** is first mixed with $FeClO_4$ in ether. To this mixture is added triethylamine which then forms metal complex **28**.

III. Assays for Modulators of Potassium Ion Channels

[0108] SK monomers as well as SK alleles and polymorphic variants are subunits of potassium ion channels. The activity of a potassium ion channel comprising SK subunits can be assessed using a variety of *in vitro* and *in vivo* assays, *e.g.*, measuring current, measuring membrane potential, measuring ion flow, *e.g.*, potassium or rubidium, measuring potassium concentration, measuring second messengers and transcription levels, using potassium-dependent yeast growth assays, and using *e.g.*, voltage-sensitive dyes, radioactive tracers, and patch-clamp electrophysiology.

[0109] Furthermore, such assays can be used to test for inhibitors and activators of channels comprising SK. The SK family of channels is implicated in a number of disorders that are targets for a therapeutic or prophylactic regimen, which functions by blockade or inhibition of one or more members of the SK channel family. The compounds and methods of the invention are useful to treat central or peripheral nervous system disorders (*e.g.*, migraine, ataxia, Parkinson's disease, bipolar disorders, trigeminal neuralgia, spasticity, mood disorders, brain tumors, psychotic disorders, myokymia, seizures, epilepsy, hearing and vision loss, psychosis, anxiety, depression, dementia, memory and attention deficits, Alzheimer's disease, age-related memory loss, learning deficiencies, anxiety, traumatic brain injury, dysmenorrhea, narcolepsy and motor neuron diseases), and as neuroprotective agents (*e.g.*, to prevent stroke and the like). The compounds of the invention are also useful in treating disease states such as gastroesophogeal reflux disorder and gastrointestinal hypomotility disorders, irritable bowel syndrome, secretory diarrhea, asthma, cystic fibrosis,

chronic obstructive pulmonary disease and rhinorrhea, convulsions, vascular spasms, coronary artery spasms, renal disorders, polycystic kidney disease, bladder spasms, urinary incontinence, bladder outflow obstruction, ischemia, cerebral ischemia, ischemic heart disease, angina pectoris, coronary heart disease, Reynaud's disease, intermittent claudication, Sjorgren's syndrome, arrhythmia, hypertension, myotonic muscle dystrophia, xerostomi, diabetes type II, hyperinsulinemia, premature labor, baldness, cancer, and immune suppression.

[0110] Modulators of the potassium ion channels are tested using biologically active SK, either recombinant or naturally occurring, or by using native cells, like cells from the nervous system expressing an SK channel. SK channels can be isolated, co-expressed or expressed in a cell, or expressed in a membrane derived from a cell. In such assays, SK is expressed alone to form a homomeric potassium ion channel or is co-expressed with a second subunit (*e.g.*, another SK family member) so as to form a heteromeric potassium ion channel. Modulation is tested using one of the *in vitro* or *in vivo* assays described above. Samples or assays that are treated with a potential potassium ion channel inhibitor or activator are compared to control samples without the test compound, to examine the extent of modulation. Control samples (untreated with activators or inhibitors) are assigned a relative potassium ion channel activity value of 100. Inhibition of channels comprising SK is achieved when the potassium ion channel activity value relative to the control is less than 70%, preferably less than 40% and still more preferably, less than 30%. Compounds that decrease the flow of ions will cause a detectable decrease in the ion current density by decreasing the probability of a channel comprising SK being open, by decreasing conductance through the channel, and decreasing the number or expression of channels.

[0111] Changes in ion flow may be assessed by determining changes in polarization (*i.e.*, electrical potential) of the cell or membrane expressing the potassium ion channel. A preferred means to determine changes in cellular polarization is by measuring changes in current or voltage with the voltage-clamp and patch-clamp techniques, using the "cell-attached" mode, the "inside-out" mode, the "outside-out" mode, the "perforated cell" mode, the "one or two electrode" mode, or the "whole cell" mode (*see, e.g.*, Ackerman *et al., New Engl. J. Med.* **336**: 1575-1595 (1997)). Whole cell currents are conveniently determined using the standard methodology (*see, e.g.*, Hamil *et al., Pflugers. Archiv.* **391**: 85 (1981)). Other known assays include: radiolabeled rubidium flux assays and fluorescence assays using voltage-sensitive dyes (*see, e.g.*, Vestergarrd-Bogind *et al., J. Membrane Biol.* **88**: 67-

75 (1988); Daniel *et al., J. Pharmacol. Meth.* **25**: 185-193 (1991); Holevinsky *et al., J. Membrane Biology* **137**: 59-70 (1994)). Assays for compounds capable of inhibiting or increasing potassium flow through the channel proteins can be performed by application of the compounds to a bath solution in contact with and comprising cells having a channel of the present invention (*see, e.g.*, Blatz *et al., Nature* **323**: 718-720 (1986); Park, *J. Physiol.* **481**: 555-570 (1994)). Generally, the compounds to be tested are present in the range from about 1 pM to about 100 mM, preferably from about 1 pM to about 1 μM.

[0112] The effects of the test compounds upon the function of the channels can be measured by changes in the electrical currents or ionic flow or by the consequences of changes in currents and flow. Changes in electrical current or ionic flow are measured by either increases or decreases in flow of ions such as potassium or rubidium ions. The cations can be measured in a variety of standard ways. They can be measured directly by concentration changes of the ions or indirectly by membrane potential or by radio-labeling of the ions. Consequences of the test compound on ion flow can be quite varied. Accordingly, any suitable physiological change can be used to assess the influence of a test compound on the channels of this invention. The effects of a test compound can be measured by a toxin-binding assay. When the functional consequences are determined using intact cells or animals, one can also measure a variety of effects such as transmitter release (*e.g.*, dopamine), hormone release (*e.g.*, insulin), transcriptional changes to both known and uncharacterized genetic markers (*e.g.*, northern blots), cell volume changes (*e.g.*, in red blood cells), immunoresponses (*e.g.*, T cell activation), changes in cell metabolism such as cell growth or pH changes, and changes in intracellular second messengers such as calcium, or cyclic nucleotides.

IV. Pharmaceutical Compositions For Use as Potassium Ion Channel Modulators

[0113] In another aspect, the present invention provides pharmaceutical compositions comprising a pharmaceutically acceptable carrier and a compound of Formula I.

Formulation of the Compounds (Compositions)

[0114] The compounds of the present invention can be prepared and administered in a wide variety of oral, parenteral and topical dosage forms. Thus, the compounds of the present invention can be administered by injection, that is, intravenously, intramuscularly, intracutaneously, subcutaneously, intraduodenally, or intraperitoneally. Also, the compounds described herein can be administered by inhalation, for example, intranasally. Additionally,

the compounds of the present invention can be administered transdermally. Accordingly, the present invention also provides pharmaceutical compositions comprising a pharmaceutically acceptable carrier and either a compound of Formula I, or a pharmaceutically acceptable salt of a compound of Formula I.

[0115] For preparing pharmaceutical compositions from the compounds of the present invention, pharmaceutically acceptable carriers can be either solid or liquid. Solid form preparations include powders, tablets, pills, capsules, cachets, suppositories, and dispersible granules. A solid carrier can be one or more substances, which may also act as diluents, flavoring agents, binders, preservatives, tablet disintegrating agents, or an encapsulating material.

[0116] In powders, the carrier is a finely divided solid, which is in a mixture with the finely divided active component. In tablets, the active component is mixed with the carrier having the necessary binding properties in suitable proportions and compacted in the shape and size desired.

[0117] The powders and tablets preferably contain from 5% or 10% to 70% of the active compound. Suitable carriers are magnesium carbonate, magnesium stearate, talc, sugar, lactose, pectin, dextrin, starch, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose, a low melting wax, cocoa butter, and the like. The term "preparation" is intended to include the formulation of the active compound with encapsulating material as a carrier providing a capsule in which the active component with or without other carriers, is surrounded by a carrier, which is thus in association with it. Similarly, cachets and lozenges are included. Tablets, powders, capsules, pills, cachets, and lozenges can be used as solid dosage forms suitable for oral administration.

[0118] For preparing suppositories, a low melting wax, such as a mixture of fatty acid glycerides or cocoa butter, is first melted and the active component is dispersed homogeneously therein, as by stirring. The molten homogeneous mixture is then poured into convenient sized molds, allowed to cool, and thereby to solidify.

[0119] Liquid form preparations include solutions, suspensions, and emulsions, for example, water or water/propylene glycol solutions. For parenteral injection, liquid preparations can be formulated in solution in aqueous polyethylene glycol solution.

[0120] Aqueous solutions suitable for oral use can be prepared by dissolving the active component in water and adding suitable colorants, flavors, stabilizers, and thickening agents as desired. Aqueous suspensions suitable for oral use can be made by dispersing the finely divided active component in water with viscous material, such as natural or synthetic gums, resins, methylcellulose, sodium carboxymethylcellulose, and other well-known suspending agents.

[0121] Also included are solid form preparations, which are intended to be converted, shortly before use, to liquid form preparations for oral administration. Such liquid forms include solutions, suspensions, and emulsions. These preparations may contain, in addition to the active component, colorants, flavors, stabilizers, buffers, artificial and natural sweeteners, dispersants, thickeners, solubilizing agents, and the like.

[0122] The pharmaceutical preparation is preferably in unit dosage form. In such form the preparation is subdivided into unit doses containing appropriate quantities of the active component. The unit dosage form can be a packaged preparation, the package containing discrete quantities of preparation, such as packeted tablets, capsules, and powders in vials or ampoules. Also, the unit dosage form can be a capsule, tablet, cachet, or lozenge itself, or it can be the appropriate number of any of these in packaged form.

[0123] The quantity of active component in a unit dose preparation may be varied or adjusted from 0.1 mg to 10000 mg, more typically 1.0 mg to 1000 mg, most typically 10 mg to 500 mg, according to the particular application and the potency of the active component. The composition can, if desired, also contain other compatible therapeutic agents.

V. Methods for Decreasing Ion Flow in Potassium Ion Channels

[0124] In yet another aspect, the present invention provides a method for decreasing ion flow through potassium ion channels in a cell, comprising contacting the cell with a potassium ion channel modulating amount of a compound according to Formula I.

[0125] In an exemplary embodiment, the potassium ion channels comprise at least one SK subunit.

[0126] The methods provided in this aspect of the invention are useful in the therapy of conditions mediated through potassium ion flow, as well as for the diagnosis of conditions that can be treated by decreasing ion flow through potassium ion channels. Additionally the methods are useful for determining if a patient will be responsive to therapeutic agents which

act by modulating potassium ion channels. In particular, a patient's cell sample can be obtained and contacted with a compound of Formula I and the ion flow can be measured relative to a cell's ion flow in the absence of a compound of Formula I. A decrease in ion flow will typically indicate that the patient will be responsive to a therapeutic regiment of ion channel modulators.

VI. Methods for Treating Conditions Mediated by Potassium Ion Channels

[0127] In still another aspect, the present invention provides a method for treating a disease through the modulation of potassium ion flow through potassium ion channels. The compounds are useful in the treatment of central or peripheral nervous system disorders (*e.g.*, migraine, ataxia, Parkinson's disease, bipolar disorders, trigeminal neuralgia, spasticity, mood disorders, brain tumors, psychotic disorders, myokymia, seizures, epilepsy, hearing and vision loss, psychosis, anxiety, depression, dementia, memory and attention deficits, Alzheimer's disease, age-related memory loss, learning deficiencies, anxiety, traumatic brain injury, dysmenorrhea, narcolepsy and motor neuron diseases), and as neuroprotective agents (*e.g.*, to prevent stroke and the like). The compounds of the invention are also useful in treating disease states such as gastroesophogeal reflux disorder and gastrointestinal hypomotility disorders, irritable bowel syndrome, secretory diarrhea, asthma, cystic fibrosis, chronic obstructive pulmonary disease and rhinorrhea, convulsions, vascular spasms, coronary artery spasms, renal disorders, polycystic kidney disease, bladder spasms, urinary incontinence, bladder outflow obstruction, ischemia, cerebral ischemia, ischemic heart disease, angina pectoris, coronary heart disease, Reynaud's disease, intermittent claudication, Sjorgren's syndrome, arrhythmia, hypertension, myotonic muscle dystrophia, xerostomi, diabetes type II, hyperinsulinemia, premature labor, baldness, cancer, and immune suppression. This method involves administering, to a patient, an effective amount of a compound having Formula I.

[0128] The compounds provided herein are useful as potassium ion channel modulators and find therapeutic utility via modulation of potassium ion channels in the treatment of diseases or conditions. The potassium ion channels that are typically modulated are described herein. As noted above, these channels may include homomultimers and heteromultimers.

[0129] In therapeutic use for the treatment of epilepsy or other neurological conditions, the compounds utilized in the pharmaceutical method of the invention are administered at the initial dosage of about 0.001 mg/kg to about 1000 mg/kg daily. A daily dose range of about

0.1 mg/kg to about 100 mg/kg is more typical. The dosages, however, may be varied depending upon the requirements of the patient, the severity of the condition being treated, and the compound being employed. Determination of the proper dosage for a particular situation is within the skill of the practitioner. Generally, treatment is initiated with smaller dosages, which are less than the optimum dose of the compound. Thereafter, the dosage is increased by small increments until the optimum effect under the circumstances is reached. For convenience, the total daily dosage may be divided and administered in portions during the day.

[0130] The materials and methods of the present invention are further illustrated by the examples which follow. These examples are offered to illustrate, but not to limit, the claimed invention.

EXAMPLES

General

[0131] In the examples below, unless otherwise stated, temperatures are given in degrees Celsius (°C); operations were carried out at room or ambient temperature, "rt," or "RT," (typically a range of from about 18-25 °C; evaporation of solvent was carried out using a rotary evaporator under reduced pressure (typically, 4.5-30 mm Hg) with a bath temperature of up to 60 °C; the course of reactions was typically followed by thin layer chromatography (TLC) and reaction times are provided for illustration only; melting points are uncorrected; products exhibited satisfactory ^{1}H-NMR and/or microanalytical data; yields are provided for illustration only; and the following conventional abbreviations are also used: mp (melting point), L (liter(s)), mL (milliliters), mmol (millimoles), g (grams), mg (milligrams), min (minutes), and h (hours).

[0132] Unless otherwise specified, all solvents (HPLC grade) and reagents were purchased from suppliers and used without further purification. Reactions were conducted under a blanket of argon unless otherwise stated. Analytical TLC was performed on Whatman Inc. 60 silica gel plates (0.25 mm thickness). Compounds were visualized under UV lamp (254 nM) or by developing with $KMnO_4$/KOH, ninhydrin or Hanessian's solution. Flash chromatography was done using silica gel from Selectro Scientific (particle size 32-63). ^{1}H NMR, ^{19}F NMR and ^{13}C NMR spectra were recorded on a Varian 300 machine at 300 MHz, 282 MHz and 75.7 MHz, respectively. Melting points were recorded on a Electrothermal IA9100 apparatus and were uncorrected.

EXAMPLE 1

***Preparation of* 2 *from* 1**

1.1 Nucleophilic Replacement

[0133] A mixture of 14.7 mmol of **1** and 75 mmol of benzylamine was heated at 220°C for 6 h in a sealed tube. The reaction mixture was concentrated *in vacuo* and the residue was purified by column chromatography on silica gel to give 7.0 mmol of *N*-benzyl pyridine-2-amine.

[0134] A solution of 6.9 mmol of *N*-benzyl pyridin-2-amine in 15 mL of conc. H_2SO_4 was stirred at 80 °C for 1 h. The reaction mixture was poured into crushed ice and neutralized with 28% NH_4OH. The mixture was extracted with AcOEt and the organic phase was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel to give 5.0 mmol of **2**.

1.2 Results

[0135] Analytical data for exemplary compounds of structure **2** are provided below.

1.2.a 5-Hexylpyridin-2-ylamine

[0136] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, J = 2.2 Hz, 1H), 7.26 (dd, J_1 = 8.4 Hz, J_2 = 2.2 Hz, 1H), 6.45 (d, J = 8.4 Hz, 1H), 4.27 (br s, 2H), 2.45 (d, J = 6.6 Hz, 1H), 1.48-1.56 (m, 2H),1.27-1.35 (m, 6H), 0.88 (t, J = 6.6 Hz, 3H); MS *m/z*: 178 (M+1).

1.2.b 5-tert-Butylpyridin-2-ylamine

[0137] ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (d, J = 2.6 Hz, 1H), 7.47 (dd, J_1 = 8.6 Hz, J_2 = 2.6 Hz, 1H), 6.47 (dd, J_1 = 8.6 Hz, J_2 = 0.7 Hz, 1H), 1.28 (s, 9H); MS *m/z*: 151 (M+1).

1.2.c 5-[2-(Benzyloxy)ethyl]pyridin-2-ylamine

[0138] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (d, J = 1.8 Hz, 1H), 7.25–7.37 (m, 6H), 6.45 (dd, J_1 = 8.4 Hz, J_2 = 0.7 Hz, 1H), 4.51 (s, 2H), 4.31 (br s, 2H), 3.62 (t, J = 6.9 Hz, 2H), 2.78 (t, J = 6.9 Hz, 2H); MS *m/z*: 228 (M+1).

1.2.d 1-(6-Aminopyridin-3-yl)-4-methylpiperazin-2-one

[0139] ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.80 (d, J = 2.4 Hz, 1H), 7.28 (dd, J_1 = 8.7 Hz, J_2 = 2.7 Hz, 1H), 6.43 (d, J = 8.8 Hz, 1H), 5.97 (br s, 2H), 3.53 (t, J = 5.4 Hz, 2H), 3.06 (s, 2H), 2.68 (t, J = 5.4 Hz, 2H), 2.26 (s, 3H); MS *m/z*: 279 (M + 1).

EXAMPLE 2

***Preparation of* 2 *from* 3**

2.1 Catalytic Reduction

[0140] A solution or a suspension of 15 mmol of **3** and 0.5 g of Pd/C (10%) in 150 mL of methanol was stirred overnight under H_2 (1 atm). After filtering through celite, the solution was concentrated under a reduced pressure to give 15 mmol of **2**.

EXAMPLE 3

***Preparation of* 2**

3.1 Iodination of **4**

[0141] A mixture of 240 mmol of **4**, 58 mmol of HIO_4, and 240 mmol of I_2 in 60 mL of water, 4 mL of concentrated H_2SO_4, and 200 mL of acetic acid was stirred at 80 °C for 4 h. Excess I_2 was neutralized by the addition of 200 mL of saturated $Na_2S_2O_3$ solution. The resulting aqueous solution was extracted with EtOAc. The organic phase was washed with saturated NaCl, dried over $MgSO_4$, and concentrated under a reduced pressure. The residue was purified by column chromatography on silica gel to give 136 mmol of **5**.

3.2 Suzuki Cross Coupling

[0142] A mixture of 15 mmol of **5**, 15 mmol of **6**, 0.35 mmol of $Pd_2(dba)_3$, and 2.4 mmol of PPh_3 in 40 mL of toluene, 20 mL of ethanol, and 20 mL of water was refluxed overnight under N_2. The reaction mixture was diluted with 300 mL of ethyl acetate and the organic solution was washed with saturated NaCl, dried over $MgSO_4$, and concentrated under a reduced pressure. The residue was purified by column chromatography on silica gel to give 13.1 mmol of **2**.

3.3 Results

[0143] Analytical data for exemplary compounds of structure **2** are provided below.

3.3.a <u>*5-(2-Methoxy-phenyl)-pyridin-2-ylamine*</u>

[0144] ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.99 (d, J = 2.0 Hz, 1H), 7.48 (dd, J_1 = 8.6 Hz, J_2 = 2.3 Hz, 1H), 7.26 (d, J = 7.5 Hz, 1H), 7.21 (d, J = 6.1 Hz, 1H), 7.03 (d, J = 8.0 Hz, 1H), 6.96 (t, J = 7.3 Hz, 1H), 6.44 (d, J = 8.5 Hz, 1H), 5.94 (s, 2H), 3.73 (s, 3H); MS *m/z*: 201 (M + 1).

3.3.b (5-Methyl-furan-2-yl)-pyridin-2-ylamine

[0145] ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.17 (d, J = 2.0 Hz, 1H), 7.63-7.52 (m, 2H), 6.48 (d, J = 3.2 Hz, 1H), 6.43 (d, J = 8.7 Hz, 1H), 6.08 (s, 2H), 2.27 (s, 3H); MS *m/z*: 175 (M + 1).

3.3.c [3,3']Bipyridinyl-6-ylamine

[0146] ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.78 (d, J = 2.1 Hz, 1H), 8.44 (dd, J_1 = 4.9 Hz, J_2 = 1.6 Hz, 1H), 8.27 (d, J = 2.2 Hz, 1H), 7.94 (dt, J_1 = 8.0 Hz, J_2 = 1.9 Hz, 1H), 7.73 (dd, J_1 = 8.7 Hz, J_2 = 2.6 Hz, 1H), 7.38 (dd, J_1 = 8.7 Hz, J_2 = 2.6 Hz, 1H), 6.52 (d, J = 8.7 Hz, 1H), 6.17 (s, 2H); MS *m/z*: 172 (M + 1).

3.3.d 5-(4-Fluoro-phenyl)-4-methyl-pyridin-2-ylamine

[0147] ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.68 (s, 1H), 7.30 (dd, J_1 = 8.5 Hz, J_2 = 5.7 Hz, 2H), 7.19 (t, J = 8.9 Hz, 2H), 6.33 (s, 1H), 5.87 (s, 2H), 2.07 (s, 3H); MS *m/z*: 203 (M + 1).

3.3.e 5-(3-Fluoro-phenyl)-pyridin-2-ylamine

[0148] ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.27 (d, J = 2.3 Hz, 1H), 7.71 (d, J = 8.6 Hz, 1H), 7.42-7.38 (m, 3H), 7.08-7.01 (m, 1H), 6.49 (d, J = 8.6 Hz, 1H), 6.15 (s, 2H); MS *m/z*: 189 (M + 1).

3.3.f 5-Thiophen-2-yl-pyridin-2-ylamine

[0149] ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.19 (d, J = 2.3 Hz, 1H), 7.61 (d, J = 8.5 Hz, 1H), 7.37 (d, J = 5.1 Hz, 1H), 7.25 (d, J = 3.3 Hz, 1H), 7.04 (t, J = 4.7 Hz, 1H), 6.45 (d, J = 8.7 Hz, 1H), 6.14 (s, 2H); MS *m/z*: 177 (M + 1).

EXAMPLE 4

***Preparation of* 8 *from* 5**

4.1 Ullmann Cross-Coupling

[0150] To a solution of 50.0 mmol of **5** and 60.0 mmol of **7** in 50.0 mL of 1,4-dioxane was added 0.500 mmol of copper (I) iodide followed by the addition of 100 mmol of K_3PO_4 and 5 mmol of *trans*-cyclohexanediamine, then the resulting mixture was stirred at 100 °C for 16 h. The reaction mixture was cooled to room temperature and diluted with 500 mL of H_2O. The resulting aqueous solution was extracted with $CHCl_3$. The organic phase was washed with saturated NaCl, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography to give 43.4 mmol of **8**.

4.2 Results

[0151] Analytical data for exemplary compounds of structure **8** are provided below.

4.2.a tert-Butyl 4-(6-aminopyridin-3-yl)-3-oxopiperazine-1-carboxylate

[0152] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-8.00 (m, 1H), 7.35-7.40 (m, 1H), 6.50-6.54 (m, 1H), 4.54 (br s, 2H), 4.24 (s, 2H), 3.65-3.69 (m, 2H), 3.75-3.80 (m, 2H), 1.50 (s, 9H); MS *m/z*: 293 (M+1).

4.2.b 5-(4-Methyl-1,4-diazepan-1-yl)pyridin-2-ylamine

[0153] ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.46 (d, J= 3.5 Hz, 1H), 6.95 (dd, J_1 = 8.8 Hz, J_2 = 3.5 Hz, 1H), 6.38 (d, J = 8.8Hz, 1H), 5.04 (br s, 2H), 3.26-3.40 (m, 4H), 2.53-2.59 (m, 2H), 2.41-2.47 (m, 2H), 2.24 (s, 3H), 1.78-1.90 (m, 2H); MS *m/z*: 207 (M+1).

4.2.c 4-(6-Aminopyridin-3-yl)-1-methyl-1,4-diazepan-5-one

[0154] ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.71 (d, J = 2.9 Hz, 1H), 7.18 (dd, J_1 = 8.8 Hz, J_2 = 2.9 Hz, 1H), 6.41 (d, J = 8.8 Hz, 1H), 5.90 (br s, 2H), 3.64-3.71 (m, 2H), 2.51-2.62 (m, 4H), 2.26 (s, 3H); MS *m/z*: 221(M+1).

4.2.d tert-Butyl 4-(6-aminopyridin-3-yl)-5-oxo-1,4-diazepane-1-carboxylate

[0155] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 2.8 Hz, 1H), 7.29 (dd, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 1H), 6.50 (d, J = 8.8 Hz, 1H), 4.54 (br s, 2H), 3.71–3.75 (m, 6H), 2.80–2.83 (m, 2H), 1.49 (s, 9H); MS *m/z*: 307 (M+1).

EXAMPLE 5

***Preparation of* 8**

5.1 Buchwald Cross-Coupling

[0156] A mixture of 30 mmol of **9**, 30 mmol of **7**, 0.04 mmol of $Pd_2(dba)_3$, 0.08 mmol of *rac*-2,2'-bis(phenylphosphino)-1,1'-binaphthyl (BINAP), and 42 mmol of Cs_2CO_3 in 100 mL of dry toluene was stirred at 80 °C for two days under N_2. The reaction mixture was diluted with 400 mL of ethyl acetate and the organic solution was washed with saturated NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was crystallized in ethyl acetate to yield 15.8 mmol of **10**.

[0157] A solution or a suspension of 15 mmol of **10** and 0.5 g of Pd/C (10%) in 150 mL of methanol was stirred overnight under H_2 (1 atm). After filtering through celite, the solution was concentrated under a reduced pressure to give 15 mmol of **8**.

5.2 Results

[0158] Analytical data for exemplary compounds of structure **8** are provided below.

5.2.a 5-(4-Methyl-piperazin-1-yl)-pyridin-2-ylamine

[0159] ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.56 (d, J = 2.7 Hz, 1H), 7.13 (dd, J_1 = 8.9 Hz, J_2 = 2.9 Hz, 1H), 6.36 (d, J = 8.8 Hz, 1H), 5.36 (s, 2H), 2.89 (t, J = 5.0 Hz, 4H), 2.40 (t, J = 5.0 Hz, 4H), 2.18 (s, 3H); MS *m/z*: 193 (M + 1).

5.2.b 4-Methyl-3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-ylamine

[0160] ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.56 (d, J = 2.8 Hz, 1H), 7.11 (dd, J_1 = 8.9 Hz, J_2 = 3.0 Hz, 1H), 6.35 (d, J = 8.8 Hz, 1H), 5.34 (s, 2H), 3.26 (d, J = 12.0 Hz, 2H), 2.45 (dt, J_1 = 9.3 Hz, J_2 = 4.2 Hz, 2H), 1.64 (d, J = 12.5 Hz, 2H), 1.4-1.3 (m, 1H), 1.44-1.28 (m, 2H), 0.90 (d, J = 6.5 Hz, 3H); MS *m/z*: 192 (M + 1).

5.2.c 1-(6-Aminopyridin-3-yl)-pyrrolidin-2-one

[0161] ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.03 (d, J = 2.6 Hz, 1H), 7.63 (dd, J_1 = 8.9 Hz, J_2 = 2.6 Hz, 1H), 6.42 (d, J = 8.9 Hz, 1H), 5.83 (s, 2H), 3.70 (t, J = 7.0 Hz, 2H), 2.39 (t, J_1 = 7.8 Hz, 2H), 2.01 (dd, J_1 = 7.1 Hz, J_2 = 7.9 Hz, 2H); MS *m/z*: 178 (M + 1).

5.2.d 1-(6-Aminopyridin-3-yl)piperidin-2-one

[0162] ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.76 (d, J = 2.4 Hz, 1H), 7.24 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1H), 6.42 (d, J = 8.8 Hz, 1H), 5.90 (br s, 2H), 3.49 (t, J = 6.0 Hz, 2H), 2.34 (t, J = 6.0 Hz, 2H), 1.77-1.85 (m, 4H),; MS *m/z*: 192 (M + 1).

5.2.e 1-(6-Aminopyridin-3-yl)piperidin-4-ol

[0163] ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.59 (d, J = 2.4 Hz, 1H), 7.14 (dd, J_1 = 9.2 Hz, J_2 = 2.4 Hz, 2H), 6.38 (d, J = 9.2 Hz, 1H), 5.34 (br s, 2H), 4.63 (1H, d, J = 4.4 Hz), 3.50-3.57 (m, 1H), 3.18-3.23 (m, 2H), 2.59-2.65 (m, 2H), 1.76-1.83 (m, 2H), 1.44-1.54 (m, 2H); MS *m/z*: 194 (M + 1).

5.2.f *5-Piperidin-1-ylpyridin-2-ylamine*

[0164] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 2.8 Hz, 1H), 7.17 (dd, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 1H), 6.47 (dd, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1H), 4.11 (br s, 2H), 2.98 (d, J = 5.2 Hz, 2H), 2.97 (d, J = 5.2 Hz, 2H), 1.68-1.74 (m, 4H), 1.51-1.57 (m, 2H); MS *m/z*: 178 (M + 1).

5.2.g *5-(4-Isopropylpiperazin-1-yl)pyridin-2-ylamine*

[0165] ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.55-7.60 (m, 1H), 7.10-7.17 (m, 1H), 6.35-6.42 (m, 1H), 5.34 (br s, 2H), 2.85-2.94 (m, 4H), 2.50-2.70 (m, 5H), 0.95-1.02 (m, 6H); MS *m/z*: 221 (M + 1).

5.2.h *tert-Butyl 4-(6-aminopyridin-3-yl)piperazine-1-carboxylate*

[0166] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 2.8 Hz, 1H), 7.17 (dd, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 1H), 6.49 (d, J = 8.8 Hz, 1H), 4.21 (br s, 2H), 3.57 (t, J = 5.2 Hz, 4H), 2.96 (t, J = 5.2 Hz, 4H), 1.48 (s, 9H); MS *m/z*: 279 (M + 1).

5.2.i *1-(6-Aminopyridin-3-yl)-4-methylpiperazin-2-one*

[0167] ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.80 (d, J = 2.4 Hz, 1H), 7.28 (dd, J_1 = 8.7 Hz, J_2 = 2.7 Hz, 1H), 6.43 (d, J = 8.8 Hz, 1H), 5.97 (br s, 2H), 3.53 (t, J = 5.4 Hz, 2H), 3.06 (s, 2H), 2.68 (t, J = 5.4 Hz, 2H),2.26 (s, 3H); MS *m/z*: 207 (M + 1).

5.2.j *5-[3-(Dimethylamino)pyrrolidin-1-yl]pyridin-2-ylamine*

[0168] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 2.8 Hz, 1H), 6.83 (dd, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 1H), 6.49 (d, J = 8.8 Hz, 1H), 3.96 (br s, 2H), 3.24-3.41 (m, 3H), 3.09 (t, J = 8.0 Hz, 1H), 2.82-2.90 (m, 1H), 2.35 (s, 6H), 2.14-2.22 (m, 1H), 1.86-1.96 (m, 1H); MS *m/z*: 206 (M + 1).

5.2.k *N^5-1-Azabicyclo[2.2.2]oct-3-ylpyridin-2,5-yldiamine*

[0169] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 2.8 Hz, 1H), 6.86 (dd, J_1 = 8.4 Hz, J_2 = 2.8 Hz, 1H), 6.44 (d, J = 8.4 Hz, 1H), 4.00 (br s, 2H), 3.34-3.37 (m, 1H), 2.80-2.90 (m, 4H), 2.50-2.53 (m, 1H), 1.23-1.97 (m, 6H); MS *m/z*: 218 (M + 1).

5.2.l *5-(2,4,5-Trimethylpiperazin-1-yl)pyridin-2-ylamine*

[0170] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 2.8 Hz, 1H), 7.30 (dd, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 1H), 6.49 (d, J = 8.8 Hz, 1H), 4.29 (br s, 2H), 3.06 (m, 1H), 2.86 (dd, J_1 = 11.2 Hz, J_2 = 3.2 Hz, 2H), 2.66 (m, 1H), 2.33 (m, 4H), 2.12 (t, J = 10.8 Hz, 1H), 1.07 (d, J = 6.4 Hz, 3H), 0.85 (d, J = 6.4 Hz, 3H); MS *m/z*: 221 (M + 1).

5.2.m *N^5-Methyl-N^5-(1-methylpyrrolidin-3-yl)pyridin-2,5-yldiamine*

[0171] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 2.8 Hz, 1H), 7.16 (dd, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 1H), 6.47 (d, J = 8.8 Hz, 1H), 4.12 (br s, 2H), 3.97-4.04 (m, 1H), 2.72 (s, 3H), 2.60-2.70 (m, 2H), 2.50-2.56 (m, 2H), 2.34 (s, 3H), 2.04-2.10 (m, 1H), 1.77-1.83 (m, 1H); MS *m/z*: 207 (M + 1).

5.2.n *5-(3-Methylpiperazin-1-yl)pyridin-2-ylamine*

[0172] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 2.8 Hz, 1H), 7.15 (dd, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 1H), 6.48 (d, J = 8.8 Hz, 1H), 4.33 (m, 1H), 4.21 (br s, 2H), 3.92-3.96 (m, 1H), 3.19-3.26 (m, 2H), 3.08-3.11 (m, 1H), 2.82 (dd, J_1 = 11.6 Hz, J_2 = 4.0 Hz, 1H), 2.61-2.68 (m, 1H), 1.48 (s, 9H), 1.32 (d, J = 6.8 Hz, 3H); MS *m/z*: 293 (M + 1).

5.2.o *5-(3,5-Dimethylpiperazin-1-yl)pyridin-2-ylamine*

[0173] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 2.8 Hz, 1H), 7.16 (dd, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 1H), 6.50 (d, J = 8.8 Hz, 1H), 4.18-4.24 (m, 2H), 3.08-3.11 (m, 2H), 2.80 (dd, J_1 = 11.6 Hz, J_2 = 4.0 Hz, 1H), 1.49 (s, 9H), 1.37 (d, J = 6.8 Hz, 6H); MS *m/z*: 307 (M+1).

5.2.p *N^5-(2-Methoxyethyl)-N^5-methylpyridin-2,5-yldiamine*

[0174] MS *m/z*: 182 (M+1).

5.2.q *5-(4-Methoxypiperidin-1-yl)pyridin-2-ylamine*

[0175] MS *m/z*: 208 (M+1).

EXAMPLE 6

***Preparation of* 8**

6.1 Ullmann Cross-Coupling

[0176] To a solution of 24.6 mmol of **9** and 27.3 mmol of **7** in 50 mL of 1,4-dioxane was added 4.92 mmol of copper (I) iodide followed by the addition of 49.2 mmol of K_3PO_4 and 4.92 mmol of *trans*-cyclohexanediamine, then the resulting mixture was stirred at 100°C for 12 h. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. The residue was diluted with $CHCl_3$, poured into water, and insoluble material was removed by celite filtration. The filtrate was extracted with $CHCl_3$, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography to give 7.87 mmol of nitro derivative.

[0177] A solution of 7.66 mmol of nitro derivative and 0.5 g of Pd/C (10%) in 150 mL of methanol was stirred overnight under H_2 (1 atm). After filtering through celite, the solution was concentrated under reduced pressure to give 4.75 mmol of **8**.

6.2 Results

[0178] Analytical data for an exemplary compound of structure **8** are provided below.

6.2.a 4-(6-Aminopyridin-3-yl)-1-benzyl-1,4-diazepan-5-one

[0179] ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.70 (d, J = 2.4 Hz, 1H), 7.17 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1H), 7.30-7.36 (m, 5H), 6.40 (d, J = 8.8 Hz, 1H), 5.90 (br s, 2H), 3.66-3.72 (m, 2H), 3.59 (br s, 2H), 2.59-2.71 (m, 6H); MS *m/z*: 327 (M+1).

EXAMPLE 7

***Preparation of* 12**

7.1 Halogenation

[0180] To a solution of 30.7 mmol of **2** and 5 mL of bromine in 48 mL of hydrobromic acid (48%) at 0 °C was added 24 mL (25 M) of aqueous $NaNO_2$. The mixture was stirred for 1 h at rt before it was neutralized by 145 mL of 3M NaOH. The aqueous solution was extracted with ethyl acetate, and the organic phase was washed with saturated NaCl, dried over $MgSO_4$, and concentrated under a reduced pressure. The crude product was purified by column chromatography to give 24.6 mmol of **12**.

7.2 Results

[0181] Analytical data for exemplary compounds of structure **12** are provided below.

7.2.a 2-Bromo-5-chloro-pyridine

[0182] ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.47 (d, J = 2.8 Hz, 1H), 7.89 (dd, J_1 = 8.5 Hz, J_2 = 2.7 Hz, 1H), 7.69 (d, J = 8.5 Hz, 1H); MS *m/z*: 192 (M + 1).

7.2.b 2-Bromo-5-(4-fluoro-phenyl)-pyridine

[0183] ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.68 (d, J = 2.4 Hz, 1H), 8.03 (dd, J_1 = 8.3 Hz, J_2 = 2.6 Hz, 1H), 7.80-7.70 (m, 3H), 7.34 (d, J = 6.6 Hz, 1H), 7.32 (d, J = 6.8 Hz, 1H); MS *m/z*: 252 (M + 1).

EXAMPLE 8

***Preparation of* 14**

8.1 Stannylation

[0184] To a solution of 17.4 mmol of **13** in 60 mL of dry THF at -78 °C under N_2 was added 19.2 mmol of *n*-BuLi (2.5 M in hexane), and the resulting brown solution was stirred for 30 min before 20.9 mmol of Bu_3SnCl was added. The reaction mixture was allowed to warm to room temperature overnight. After the reaction was quenched with saturated NH_4Cl and the mixture was extracted with ethyl acetate, the combined organic phase was washed with saturated NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel to give 10.5 mmol of **14**.

8.2 Results

[0185] Analytical data for exemplary compounds of structure **14** are provided below.

8.2.a 4-Methyl-2-tributylstannanyl-pyridine

[0186] ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (d, J = 5.0 Hz, 1H), 7.21 (s, 1H), 6.93 (d, J = 4.7 Hz, 1H), 2.29 (s, 3H), 1.61-1.47 (m, 6H), 1.39-1.29 (m, 6H), 1.16-1.08 (m, 6H), 0.87 (t, J = 7.3 Hz, 9H); MS *m/z*: 384 (M + 1).

8.2.b 2-Methoxy-6-tributylstannanyl-pyridine

[0187] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (dd, J_1 = 8.3 Hz, J_2 = 6.9 Hz, 1H), 6.98 (d, J = 6.1 Hz, 1H), 6.55 (d, J = 8.4 Hz, 1H), 3.93 (s, 3H), 1.62-1.53 (m, 6H), 1.38-1.27 (m, 6H), 1.12-1.05 (m, 6H), 0.89 (t, J = 5.9 Hz, 9H); MS *m/z*: 400 (M + 1).

8.2.c 5-Methyl-2-tributylstannanyl-pyridine

[0188] ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (s, 1H), 7.30-7.24 (m, 2H), 2.25 (s, 3H), 1.58-1.44 (m, 6H), 1.36-1.25 (m, 6H), 1.11-1.04 (m, 6H), 0.86 (t, J = 7.1 Hz, 9H); MS *m/z*: 384 (M + 1).

8.2.d 4-Pyrrolidin-1-yl-2-tributylstannanyl-pyridine

[0189] ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.14 (d, J = 4.5 Hz, 1H), 6.68-6.64 (m, 1H), 6.59 (d, J = 2.4 Hz, 1H), 3.41-3.39 (m, 4H), 1.97 (bs, 4H), 1.58-1.41 (m, 6H), 1.38-1.22 (m, 6H), 1.20-1.00 (m, 6H), 0.83 (t, J = 7.3 Hz, 9H); MS *m/z*: 439 (M + 1).

EXAMPLE 9

***Preparation of* 16**

9.1 Stille Cross-Coupling

[0190] A mixture of 30 mmol of **15**, 30 mmol of **14**, and 1.5 mmol of $Pd(PPh_3)_4$ in 250 mL of dry toluene was stirred at 70 °C for 2 days under N_2. The reaction was quenched with 100 mL of saturated NH_4Cl. After the mixture was extracted with EtOAc, the organic phase was washed with saturated NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography to give 17.6 mmol of **16**.

9.2 Results

[0191] Analytical data for exemplary compounds of structure **16** are provided below.

9.2.a *6-Bromo-[2,2']bipyridinyl*

[0192] ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.68 (d, J = 4.7 Hz, 1H), 8.37 (d, J = 7.6 Hz, 1H), 8.25 (d, J = 8.0 Hz, 1H), 7.95 (dt, J_1 = 7.8 Hz, J_2 = 1.7 Hz, 1H), 7.89 (t, J = 7.9 Hz, 1H), 7.69 (d, J = 7.9 Hz, 1H), 7.50-7.46 (m, 1H); MS *m/z*: 235 (M + 1).

9.2.b *2-Bromo-6-thiazol-2-yl-pyridine*

[0193] ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.10 (d, J = 7.7 Hz, 1H), 7.99 (d, J = 3.1 Hz, 1H), 7.91 (d, J = 3.1 Hz, 1H), 7.87 (t, J = 7.8 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H); MS *m/z*: 241 (M + 1).

9.2.c *2-(6-Bromo-pyridin-2-yl)-pyrazine*

[0194] ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.39 (d, J = 1.2 Hz, 1H), 8.75 (s, 2H), 8.32 (d, J_1 = 7.7 Hz, 1H), 7.94 (t, J = 7.8 Hz, 1H), 7.77 (dd, J_1 = 8.0 Hz, J_2 = 0.7 Hz, 1H); MS *m/z*: 236 (M + 1).

EXAMPLE 10

***Preparation of* 16**

10.1 Negishi Cross-Coupling

[0195] A mixture of 528 mmol of zinc dust and 47.5 mmol of 1,2-dibromoethane was heated with a heat gun until the evolution of ethylene gas was done twice. To a suspension 21.1 mmol of trimethylsilyl chloride and 176 mmol of **12** in 70.0 mL of THF were added. After 30 min 211 mmol of **15** and 2.28 mmol of $Pd(PPh_3)_4$ in 350 mL of THF were added and

the mixture was stirred for 17 h at reflux. The reaction was quenched with saturated NaCl, and insoluble material was removed by celite filtration. The filtrate was extracted with toluene, wased with saturated NaCl, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography to give 105 mmol of **16**.

10.2 Results

[0196] Analytical data for exemplary compounds of structure **16** are provided below.

10.2.a *2-Bromo-3-methoxy-6-(1,3-thiazol-2-yl)pyridine*

[0197] ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.12 (d, J = 7.8 Hz, 1H), 7.94 (d, J = 3.2 Hz, 1H), 7.83 (d, J = 3.2 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H), 3.97 (s, 3H); MS *m/z*: 275 (M+1).

10.2.b *2-Bromo-6-(5-methyl-1,3-thiazol-2-yl)pyridine*

[0198] ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.08 (dd, J_1 = 7.8 Hz, J_2 = 0.8 Hz, 1H), 7.88 (t, J = 7.8 Hz, 1H), 7.69-7.74 (m, 2H), 2.51 (d, J = 2.0 Hz, 3H); MS *m/z*: 259 (M+1).

10.2.c *2-Bromo-6-(5-ethyl-1,3-thiazol-2-yl)pyridine*

[0199] ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.08 (dd, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1H), 7.89 (t, J = 8.0 Hz, 1H), 7.75 (t, J = 0.8 Hz, 1H), 7.70 (dd, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1H), 2.91 (qd, J = J_1 = 7.6 Hz, J_2 = 0.8 Hz, 2H), 1.30 (t, J = 7.6 Hz, 3H); MS *m/z*: 272 (M+1).

10.2.d *2-Bromo-6-(5-isopropyl-1,3-thiazol-2-yl)pyridine*

[0200] ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.09 (dd, J_1 = 7.8 Hz, J_2 = 0.8 Hz, 1H), 7.89 (t, J = 7.8 Hz, 1H), 7.76 (d, J = 0.8 Hz, 1H), 7.71 (dd, J_1 = 7.8 Hz, J_2 = 0.8 Hz, 1H), 3.28 (sept, J = 6.8 Hz, 1H), 1.34 (d, J = 6.8 Hz, 6H); MS *m/z*: 284 (M+1).

10.2.e *2-Bromo-6-(5-chloro-1,3-thiazol-2-yl)pyridine*

[0201] ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (d, J = 7.6 Hz, 1H), 8.07 (s, 1H), 7.94 (t, J = 7.6 Hz, 1H), 7.78 (d, J = 7.6 Hz, 1H); MS *m/z*: 278 (M+1).

10.2.f *2-Bromo-6-(5-chloro-1,3-thiazol-2-yl)-3-methoxypyridine*

[0202] ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.07 (d, J = 8.6 Hz, 1H), 7.97 (s, 1H), 7.69 (d, J = 8.6 Hz, 1H), 3.97 (s, 3H); MS *m/z*: 308 (M+1).

EXAMPLE 11

***Preparation of* 17**

11.1 Buchwald Cross-Coupling

[0203] A mixture of 40 mmol of **15**, 40 mmol of **2** or **8**, 0.8 mmol of $Pd_2(dba)_3$, 1.6 mmol of dppp, and 60 mmol of NaOtBu in 360 mL of dry toluene was stirred at 80 °C overnight under N_2. The reaction was quenched with 100 mL of water and the mixture was diluted with 300 mL of ethyl acetate. After separating the two phases, the organic phase was washed with saturated NaCl, dried over $MgSO_4$, and concentrated under a reduced pressure. The crude product was purified by column chromatography on silica gel to give 30.7 mmol of **17**.

11.2 Results

[0204] Analytical data for exemplary compounds of structure **17** are provided below.

11.2.a (6-Bromo-pyridin-2-yl)-(5-chloro-pyridin-2-yl)-amine

[0205] ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.64 (s, 1H), 8.22 (d, J = 2.4 Hz, 1H), 7.85 (d, J = 8.9 Hz, 1H), 7.75 (d, J = 2.6 Hz, 1H), 7.05 (d, J = 2.8 Hz, 1H), 7.52 (t, J = 8.0 Hz, 1H), 7.07 (d, J = 8.0 Hz, 1H); MS *m/z*: 284 (M + 1).

EXAMPLE 12

***Preparation of* 17**

12.1 Nucleophilic Replacement

[0206] To a solution of 25.9 mmol of **15** in 50 mL of anhydrous THF was added 38.9 mmol of NaH (60% in mineral oil) followed by the addition of 25.9 mmol of **2** or **8**, and the resulting mixture was stirred at 50 °C for 8 h. After the reaction was quenched with methanol, the solvent was removed. The residue was dissolved in 100 mL of ethyl acetate and the organic solution was washed with saturated NaCl, dried over $MgSO_4$, and concentrated under a reduced pressure. The crude product was purified by column chromatography on silica gel to give 16.3 mmol of **17**.

12.2 Results

[0207] Analytical data for exemplary compounds of structure **17** are provided below.

12.2.a 6-Chloro-3-nitro-N-pyridin-2-ylpyridin-2-amine

[0208] ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.64 (br s, 1H), 8.52 (d, J = 8.4 Hz, 1H), 8.37-8.42 (m, 2H), 7.78 (t, J = 8.4 Hz, 1H), 7.07-7.11 (m, 1H), 6.92 (d, J = 8.4 Hz, 1H); MS *m/z*: 253 (M + 1).

EXAMPLE 13

***Preparation of* 18**

13.1 Nucleophilic Replacement

[0209] To a solution of 10 mmol of **2** or **8** in 100 mL of anhydrous THF was added 30 mmol of NaH (60% in mineral oil) followed by the addition of 12.5 mmol of **16**, and the resulting mixture was stirred at 100 °C overnight under N_2. After the reaction was quenched with methanol, the solvents were removed. The residue was dissolved in 100 mL of ethyl acetate and the organic solution was washed with saturated NaCl, dried over $MgSO_4$, and concentrated under a reduced pressure. The crude product was purified by column chromatography on silica gel to give 4.5 mmol of **18**.

[0210] Most of **18** was converted to an HCl salt by adding excess 4 M of HCl in 1,4-dioxane to a solution of **18** in MeOH. The pure salts were obtained by removing the solvents under reduced pressure or crystallizing in ethyl acetate.

13.2 Results

[0211] Analytical data for exemplary compounds of structure **18** are provided below.

13.2.a [5-(3-Fluoro-phenyl)-pyridin-2-yl]-(6-thiazol-2-yl-pyridin-2-yl)-amine · 2HCl

[0212] ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.17 (s, 1H), 8.84 (d, J = 2.1 Hz, 1H), 8.55 (dd, J_1 = 9.0 Hz, J_2 = 2.3 Hz, 1H), 8.05-7.97 (m, 4H), 7.83 (d, J = 7.5 Hz, 1H), 7.71-7.63 (m, 2H), 7.57 (d, J = 6.6 Hz, 1H), 7.52 (d, J = 7.5 Hz, 1H), 7.25 (dt, J_1 = 8.5 Hz, J_2 = 2.3 Hz, 1H); MS *m/z*: 349 (M + 1).

13.2.b [3,3']Bipyridinyl-6-yl-(6-thiazol-2-yl-pyridin-2-yl)-amine · 2HCl

[0213] ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.68 (s, 1H), 9.32 (d, J = 2.1 Hz, 1H), 8.93-8.84 (m, 3H), 8.39 (dd, J_1 = 9.1 Hz, J_2 = 2.6 Hz, 1H), 8.21 (d, J = 8.9 Hz, 1H), 8.10 (dd, J_1 = 8.2 Hz, J_2 = 5.8 Hz, 1H), 8.00 (d, J = 3.3 Hz, 1H), 7.91 (d, J = 3.1 Hz, 1H), 7.88 (d, J = 7.9 Hz, 1H), 7.71 (d, J = 7.1 Hz, 1H), 7.63 (d, J = 8.2 Hz, 1H); MS *m/z*: 332 (M + 1).

13.2.c (5-Phenyl-2H-pyrazol-3-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine · 2HCl

[0214] ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.50 (s, 1H), 7.99 (d, J = 3.0 Hz, 1H), 7.91 (d, J = 3.0 Hz, 1H), 7.82-7.68 (m, 3H), 7.57 (d, J = 7.3 Hz, 1H), 7.51-7.46 (m, 2H), 7.39 (d, J = 7.1 Hz, 1H), 7.21 (d, J = 8.4 Hz, 1H), 7.07 (s, 1H); MS *m/z*: 320 (M + 1).

13.2.d 1-[6-(6-Thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-pyrrolidin-2-one · 2HCl

[0215] ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.92 (s, 1H), 8.73 (d, J = 2.5 Hz, 1H), 8.40 (dd, J_1 = 9.5 Hz, J_2 = 2.6 Hz, 1H), 8.03 (d, J = 3.2 Hz, 1H), 8.01-7.92 (m, 3H), 7.78 (d, J = 7.3 Hz, 1H), 7.43 (d, J = 8.2 Hz, 1H), 3.87 (t, J = 7.1 Hz, 2H), 2.49 (t, J = 9.1 Hz, 2H), 2.15-2.05 (m, 2H); MS *m/z*: 338 (M + 1).

13.2.e [5-(4-Methyl-piperazin-1-yl)-pyridin-2-yl]-(6-pyrazin-2-yl-pyridin-2-yl)-amine · 2HCl

[0216] ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.19 (s, 1H), 9.58 (s, 1H), 8.92 (s, 1H), 8.83 (d, J = 2.4 Hz, 1H), 8.17-8.10 (m, 3H), 8.01 (d, J = 9.2 Hz, 1H), 7.59 (d, J = 9.4 Hz, 1H), 7.49 (d, J = 7.8 Hz, 1H), 3.88 (d, J = 11.2 Hz, 2H), 3.52 (d, J = 11.8 Hz, 2H), 3.26-3.16 (m, 4H), 2.80 (d, J = 4.4 Hz, 3H); MS *m/z*: 348 (M + 1).

13.2.f [2,2']Bipyridinyl-6-yl-[5-(4-fluorophenyl)-4-methyl-pyridin-2-yl]-amine

[0217] ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.82 (s, 1H), 8.67 (d, J = 3.8 Hz, 1H), 8.34 (d, J = 7.9 Hz, 1H), 8.05 (s, 1H), 7.97 (dt, J_1 = 7.7 Hz, J_2 = 1.7 Hz, 1H), 7.92 (s, 1H), 7.87 (d, J = 7.3 Hz, 1H), 7.79 (t, J = 8.2 Hz, 1H), 7.68 (d, J = 7.5 Hz, 1H), 7.46-7.41 (m, 3H), 7.29 (d, J = 8.8 Hz, 1H), 7.26 (d, J = 8.9 Hz, 1H), 2.28 (s, 3H); MS *m/z*: 357 (M + 1).

13.2.g (5-Isopropyl-pyridin-2-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine · 2HCl

[0218] ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.79 (s, 1H), 9.57 (d, J = 1.1 Hz, 1H), 8.87 (d, J = 1.2 Hz, 1H), 8.81 (d, J = 2.4 Hz, 1H), 8.39 (d, J = 2.4 Hz, 1H), 8.24 (dd, J_1 = 9.1 Hz, J_2 = 2.1 Hz, 1H), 8.18-8.12 (m, 2H), 7.66 (d, J = 9.0 Hz, 1H), 7.50 (dd, J_1 = 6.3 Hz, J_2 = 2.8 Hz, 1H), 3.07-2.98 (m, 1H), 1.25 (d, J = 7.0 Hz, 6H); MS *m/z*: 292 (M + 1).

13.2.h [5-(5-Methyl-furan-2-yl)-pyridin-2-yl]-(6-thiazol-2-yl-pyridin-2-yl)-amine · 2HCl

[0219] ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.99 (s, 1H), 8.59 (d, J = 1.9 Hz, 1H), 8.16 (d, J = 7.0 Hz, 1H), 8.01 (d, J = 2.6 Hz, 1H), 8.00 (d, J = 2.9 Hz, 1H), 7.95-7.84 (m, 2H), 7.72 (d, J

= 7.5 Hz, 1H), 7.50 (d, J = 8.3 Hz, 1H), 6.88 (d, J = 3.1 Hz, 1H), 6.22 (d, J = 2.6 Hz, 1H), 2.34 (s, 3H); MS *m/z*: 335 (M + 1).

13.2.i (5-Morpholin-4-yl-pyridin-2-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine · 2HCl

[0220] ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.36 (s, 1H), 9.57 (s, 1H), 8.97 (d, J = 1.4 Hz, 1H), 8.83 (d, J = 2.4 Hz, 1H), 8.17-8.01 (m, 3H), 8.12 (s, 1H), 7.54 (d, J = 9.2 Hz, 1H), 7.44 (dd, J_1 = 7.5 Hz, J_2 = 1.6 Hz, 1H), 3.74 (dd, J_1 = 9.2 Hz, J_2 = 4.2 Hz, 4H); 3.18 (dd, J_1 = 9.2 Hz, J_2 = 4.7 Hz, 4H); MS *m/z*: 335 (M + 1).

13.2.j [3,5-Bis(trifluoromethyl)-2,2'-bipyridin-6-yl](pyridin-2-yl)amine

[0221] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 4.8 Hz, 1H), 8.31 (d, J = 4.8 Hz, 1H), 8.33 (d, J = 8.0 Hz, 1H), 8.23 (s, 1H), 7.87 (t, J = 7.6 Hz, 1H), 7.86 (t, J = 7.6 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.65 (t, J = 7.6 Hz, 1H), 7.44 (dd, J = 4.8, 7.6 Hz, 1H), 7.00 (t, J = 7.6 Hz, 1H); MS *m/z*: 385 (M + 1).

EXAMPLE 14

***Preparation of* 18**

14.1 Buchwald Cross-Coupling

[0222] A mixture of 1.1 mmol of **16**, 1.2 mmol of **2** or **8**, 0.045 mmol of $Pd_2(dba)_3$, 0.09 mmol of dppp, and 1.58 mmol of NaO*t*Bu in 10 mL of dry toluene was stirred at 70 °C overnight under N_2. The reaction was quenched with water and the mixture was diluted with 150 mL of ethyl acetate. After separating the two phases, the organic phase was washed with saturated NaCl, dried over $MgSO_4$, and concentrated under a reduced pressure. The crude product was purified by column chromatography on silica gel to give 0.97 mmol of **18**.

[0223] Most of **18** were converted to HCl salt by adding excess 4 M of HCl in 1,4-dioxane to a solution of **18** in MeOH. The pure salts were obtained by removing the solvents under reduced pressure or crystallizing in ethyl acetate.

14.2 Results

[0224] Analytical data for exemplary compounds of structure **18** are provided below.

14.2.a [2,2']Bipyridinyl-6-yl-pyridin-2-yl-amine · 3HCl

[0225] ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.83 (s, 1H), 8.92 (d, J = 4.7 Hz, 1H), 8.56 (d, J = 5.4 Hz, 1H), 8.49 (d, J = 7.9 Hz, 1H), 8.28-8.15 (m, 4H), 7.56 (t, J = 5.8 Hz, 1H), 7.59 (d, J = 8.5 Hz, 2H), 7.34 (t, J = 7.0 Hz, 1H); MS *m/z*: 249 (M + 1).

14.2.b [2,2']Bipyridinyl-6-yl-(5-fluoro-pyridin-2-yl)-amine · 3HCl

[0226] ^{1}H NMR (300 MHz, DMSO-d_6) δ 13.00 (s, 1H), 8.96 (d, J = 4.1 Hz, 1H), 8.66 (d, J = 2.9 Hz, 1H), 8.45 (d, J = 8.0 Hz, 1H), 8.31 (t, J = 8.0 Hz, 1H), 8.15 (d, J = 7.5 Hz, 1H), 8.13 (d, J = 7.6 Hz, 1H), 7.98 (dt, J_1 = 8.7 Hz, J_2 = 3.0 Hz, 1H), 7.71-7.64 (m, 2H), 7.58 (d, J = 9.2 Hz, 1H); MS *m/z*: 267 (M + 1).

14.2.c [2,2']Bipyridinyl-6-yl-(5-chloro-pyridin-2-yl)-amine · 3HCl

[0227] ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.80 (s, 1H), 8.87 (d, J = 4.4 Hz, 1H), 8.42 (d, J = 6.3 Hz, 2H), 8.22-8.12 (m, 3H), 7.69 (dd, J_1 = 7.2 Hz, J_2 = 6.2 Hz, 1H), 7.56 (d, J = 7.8 Hz, 1H), 7.42 (s, 1H), 7.19 (d, J = 6.1 Hz, 1H); MS *m/z*: 283 (M + 1).

14.2.d [2,2']Bipyridinyl-6-yl-(3,5-dichloro-pyridin-2-yl)-amine

[0228] ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.68 (s, 1H), 8.65 (d, J = 4.2 Hz, 1H), 8.35-8.30 (m, 2H), 8.18 (d, J = 2.3 Hz, 1H), 8.0-7.86 (m, 4H), 7.42 (dd, J_1 = 6.2 Hz, J_2 = 4.7 Hz, 1H); MS *m/z*: 317 (M + 1).

14.2.e [2,2']Bipyridinyl-6-yl-[5-(4-fluoro-phenyl)-pyridin-2-yl]-amine

[0229] ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.94 (s, 1H), 8.67 (d, J = 3.8 Hz, 1H), 8.56 (s, 1H), 8.35 (d, J = 8.0 Hz, 1H), 8.04 (s, 1H), 8.04-8.00 (m, 1H), 7.96 (dt, J_1 = 7.7 Hz, J_2 = 1.8 Hz, 1H), 7.89 (d, J = 7.6 Hz, 1H), 7.81 (t, J = 7.5 Hz, 1H), 7.76-7.69 (m, 3H), 7.45-7.41 (m, 1H), 7.28 (d, J = 8.9 Hz, 2H); MS *m/z*: 343 (M + 1).

14.2.f [2,2']Bipyridinyl-6-yl-(4-methyl-pyridin-2-yl)-amine · 2HCl

[0230] ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.81 (s, 1H), 8.87 (d, J = 4.2 Hz, 1H), 8.43-8.40 (m, 2H), 8.21-8.12 (m, 3H), 8.68 (dd, J_1 = 7.2 Hz, J_2 = 5.3 Hz, 1H), 7.55 (d, J = 7.9 Hz, 1H), 7.41 (s, 1H), 7.19 (d, J = 6.1 Hz, 1H), 2.45 (s, 3H); MS *m/z*: 263 (M + 1).

14.2.g N,N-Dipyridin-2-yl-2,2'-bipyridin-6-amine dihydrochloride

[0231] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, J = 4.8 Hz, 1H), 8.50 (d, J = 2.4 Hz, 1H), 8.39 (d, J = 8.4 Hz, 1H), 8.34-8.36 (m, 3H), 7.79 (t, J = 7.6 Hz, 1H), 6.56-7.63 (m, 3H), 7.27 (t, J = 4.8 Hz, 1H), 7.07 (d, J = 8.4 Hz, 2H), 6.98-7.02 (m, 2H); MS *m/z*: 326 (M + 1).

14.2.h *1-Methyl-4-(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)piperazin-2-one dihydrochloride*

[0232] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (br s, 1H), 8.08-8.12 (m, 1H), 8.06 (d, J = 2.9 Hz, 1H), 7.96-8.02 (m, 3H), 7.77-7.83 (m, 2H), 7.38 (d, J = 8.3 Hz, 1H), 3.87 (s, 2H), 3.56-3.60 (m, 2H), 3.40-3.50 (m, 2H), 2.93 (s, 3H); MS *m/z*: 367 (M + 1).

14.2.i *4-Benzyl-1-(6-{[3-methoxy-6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)piperazin-2-one dihydrochloride*

[0233] ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.76-9.04 (m, 1H), 8.48 (d, J = 9.2 Hz, 1H), 8.35 (d, J = 2.4 Hz, 1H), 7.90-7.98 (m, 2H), 7.80 (d, J = 2.9 Hz, 1H), 7.76 (d, J = 8.3 Hz, 1H), 7.62-7.72 (m, 2H), 7.46 7.58 (m, 4H), 4.49 (s, 2H), 3.45-4.35 (m, 9H); MS *m/z*: 473 (M + 1).

14.2.j *N^2-[3-Methoxy-6-(1,3-thiazol-2-yl)pyridin-2-yl]-N^5-methyl-N^5-(1-methylpyrrolidin-3-yl)pyridine-2,5-diamine trihydrochloride*

[0234] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.86 (br s, 0.6H), 11.59 (br s, 0.4H), 10.12 (br s, 1H), 8.41–8.43 (m, 1H), 8.08 (m, 1H), 7.99 (d, J = 3.0 Hz, 1H), 7.93 (d, J = 3.5 Hz, 1H), 7.78-7.81 (m, 2H), 7.58 (d, J = 8.3 Hz, 1H), 4.92 (m, 0.6H), 4.66 (m, 0.4H), 4.01 (s, 3H), 3.03-3.73 (m, 4H), 2.93-2.96 (m, 3H), 2.81–2.85 (m, 3H), 2.17–2.31 (m, 2H); MS *m/z*: 397 (M + 1).

14.2.k *3-Methoxy-6-(1,3-thiazol-2-yl)-N-[5-(2,4,5-trimethylpiperazin-1-yl)pyridin-2-yl]pyridin-2-amine trihydrochloride*

[0235] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.49 (br s, 1H), 9.78 (br s, 0.3H), 9.38 (br s, 0.7H), 8.44-8.47 (m, 1H), 7.92-8.15 (m, 3H), 7.79 (d, J = 8.3 Hz, 1H), 7.76 (d, J = 3.4 Hz, 1H), 7.56 (d, J = 8.3 Hz, 1H), 4.13 (m, 0.3H), 4.02 (s, 3H), 3.64 (m, 1H), 3.18–3.50 (m, 4H), 2.92 (m, 0.7H), 2.80 (m, 3H), 1.33-1.35 (m, 3H), 1.23 (m, 0.9H), 0.95 (d, J = 5.9 Hz, 2.1H); MS *m/z*: 411 (M + 1).

14.2.l *N^5-1-Azabicyclo[2.2.2]oct-3-yl-N^2-[3-methoxy-6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridine-2,5-diamine trihydrochloride*

[0236] ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.65 (br s, 1H), 10.38 (br s, 1H), 8.12 (d, J = 9.3 Hz, 1H), 7.97 (d, J = 2.9 Hz, 1H), 7.91 (dd, J_1 = 9.8 Hz, J_2 =2.9 Hz, 1H), 7.86 (d, J = 3.4 Hz, 1H), 7.83 (d, J = 8.3 Hz, 1H), 7.80 (d, J = 2.9 Hz, 1H), 7.63 (d, J = 8.3 Hz, 1H), 4.02 (s, 3H), 3.72-3.99 (m, 3H), 3.18–3.32 (m, 3H), 3.01 (m, 1H), 2.22–2.23 (m, 1H), 2.13 (m, 1H), 1.91-1.96 (m, 2H), 1.73 (m, 1H); MS *m/z*: 409 (M + 1).

14.2.m *N-{5-[3-(Dimethylamino)pyrrolidin-1-yl]pyridin-2-yl}-3-methoxy-6-(1,3-thiazol-2-yl)pyridin-2-amine dihydrochloride*

[0237] ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.82 (br s, 1H), 8.26 (d, J = 9.3 Hz, 1H), 7.95 (d, J = 2.9 Hz, 1H), 7.82 (d, J = 2.9 Hz, 1H), 7.78 (d, J = 2.5 Hz, 1H), 7.73 (d, J = 8.3 Hz, 1H), 7.64 (m, 1H), 7.53 (d, J = 8.3 Hz, 1H), 4.01 (s, 3H), 3.17-3.70 (m, 5H), 2.83, 2.84 (each s, 3H x 2), 2.50-2.51 (m, 1H), 2.30-2.32 (m, 1H); MS m/z: 397 (M + 1).

14.2.n *4-(6-{[3-Methoxy-6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)-1-methyl-1,4-diazepan-5-one dihydrochloride*

[0238] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.30-11.50 (br, 1H), 8.90-9.10 (br, 1H), 8.47 (d, 9.3 Hz, 1H), 8.34 (d, J= 2.5 Hz, 1H), 7.96 (dd, J_1 = 9.3 Hz, J_2 =2.5 Hz, 1H), 7.95 (d, J= 2.9 Hz, 1H), 7.82 (d, J= 2.9 Hz, 1H), 7.77 (d, J= 8.8 Hz, 1H), 7.55 (d, J= 8.8 Hz, 1H), 4.40-4.56 (m, 1H), 4.01 (s, 3H), 3.35-3.95 (m, 6H), 2.84 (s, 1.5H), 2.83 (s, 1.5H), 2.64-2.76 (m, 1H); MS m/z: 411 (M + 1).

14.2.o *1-(6-{[6-(5-Chloro-1,3-thiazol-2-yl)-3-methoxypyridin-2-yl]amino}pyridin-3-yl)-4-methylpiperazin-2-one hydrochloride*

[0239] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.50-11.75 (br, 1H), 8.41 (d, J = 9.0 Hz, 1H), 8.39 (s, 1H), 8.30 (d, J = 2.5 Hz, 1H), 7.92 (dd, J_1 = 9.0 Hz, J_2 =2.5 Hz, 1H), 7.91 (s, 1H), 7.64 (d J= 8.3 Hz, 1H), 7.48 (d, J = 8.3 Hz, 1H), 4.00-4.04 (m, 2H), 3.99 (s, 3H), 3.56-3.74 (m, 2H), 3.30-3.40 (m, 2H), 2.91 (s, 3H); MS m/z: 431 (M + 1).

14.2.p *5-(4-Methyl-1,4-diazepan-1-yl)-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine trihydrochloride*

[0240] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.80-12.00 (br, 1H), 11.10-11.24 (br, 1H), 8.07 (d, J = 2.9 Hz, 1H), 7.96-8.05 (m, 3H), 7.89 (d, J = 3.0 Hz, 1H), 7.83 (d, J = 9.8 Hz, 1H), 7.80 (d, J = 7.8 Hz, 1H), 7.31 (d, J = 8.3 Hz, 1H), 3.76-3.96 (m, 2H), 3.38-3.60 (m, 4H), 3.10-3.30 (m, 2H), 2.80 (s, 1.5H), 2.79 (s, 1.5H), 2.30-2.48 (m, 1H), 2.12–2.24 (m, 1H); MS m/z: 367 (M + 1).

14.2.q *N-[6-(5-Ethyl-1,3-thiazol-2-yl)pyridin-2-yl]-5-(4-methylpiperazin-1-yl)pyridin-2-amine trihydrochloride*

[0241] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.92 (br s, 1H), 11.36 (br s, 1H), 8.08-8.13 (m, 2H), 7.97 (t, J = 7.8 Hz, 1H), 7.87 (d, J = 9.3 Hz, 1H), 7.78 (s, 1H), 7.75 (d, J = 7.3 Hz, 1H), 7.36 (d, J = 8.3 Hz, 1H), 3.88 (br d, J = 11.3 Hz, 4H), 3.52 (br d, J = 11.3 Hz, 2H), 3.18-3.29 (m, 4H), 2.95 (q, J = 7.3 Hz, 2H), 2.81 (d, J = 4.4 Hz, 3H), 1.34 (t, J = 7.3 Hz, 3H); MS m/z: 381 (M + 1).

14.2.r *1-(6-{[6-(5-Ethyl-1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)piperidin-2-one monohydrochloride*

[0242] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.12 (br s, 1H), 8.47 (s, 1H), 7.91 (t, J = 7.3 Hz, 1H), 7.75 (s, 1H), 7.69 (d, J = 7.3 Hz, 1H), 7.6 (s, 2H), 7.47 (d, J = 8.3 Hz, 1H), 3.67 (t, J = 5.8 Hz, 2H), 2.93 (q, J = 7.3 Hz, 2H), 2.43 (t, J = 5.8 Hz, 2H), 1.82-1.94 (m, 4H), 1.32 (t, J = 7.3 Hz, 3H); MS m/z: 380 (M + 1).

14.2.s *N-[6-(5-Ethyl-1,3-thiazol-2-yl)pyridin-2-yl]-5-pyrrolidin-1-ylpyridin-2-amine dihydrochloride*

[0243] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.48 (br s, 1H), 7.95 (t, J= 7.8 Hz, 1H), 7.78 (s, 1H), 7.75 (br s, 1H), 7.73 (d J = 7.3 Hz, 1H), 7.63-7.68 (m, 2H), 7.20 (d, J = 8.3 Hz, 1H), 3.33 (br s, 4H), 2.95 (q, J = 7.3 Hz, 2H), 2.02 (br s, 4H), 1.33 (t, J = 7.3 Hz, 3H); MS m/z: 352 (M + 1).

14.2.t *N-[6-(5-Ethyl-1,3-thiazol-2-yl)pyridin-2-yl]-5-piperidin-1-ylpyridin-2-amine dihydrochloride*

[0244] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.14 (br s, 1H), 8.45 (br s, 1H), 8.28 (dd, J_1 = 8.8 Hz, J_2 =2.4 Hz, 1H), 8.03 (br s, 1H), 7.90 (t, J = 7.8 Hz, 1H), 7.75 (s, 1H), 7.70 (d, J = 8.6 Hz, 1H), 7.42 (d, J = 8.3 Hz, 1H), 2.92 (q, J = 7.3 Hz, 2H), 1.87 (br s, 4H), 1.63 (br s, 2H), 1.33 (t, J = 7.3 Hz, 3H); MS m/z: 366 (M + 1).

14.2.u *N-[6-(5-Methyl-1,3-thiazol-2-yl)pyridin-2-yl]-5-morpholin-4-ylpyridin-2-amine dihydrochloride*

[0245] ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.81 (brs, 1H), 10.43 (brs, 1H), 8.81-9.45 (m, 2H), 7.00-7.76 (m, 5H), 3.60-5.00 (m, 11H); MS m/z: 354 (M + 1).

14.2.v *1-(6-{[6-(5-Chloro-1,3-thiazol-2-yl)-3-methoxypyridin-2-yl]amino}pyridin-3-yl)pyrrolidin-2-one monohydrochloride*

[0246] ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.52 (br s, 1H), 8.77 (d, J = 3.0 Hz, 1H), 8.43 (dd, J_1 = 9.3 Hz, J_2 =2.4 Hz, 1H), 8.34 (d, J = 9.3 Hz, 1H), 7.94 (s, 1H), 7.72 (d, J = 8.3 Hz, 1H), 7.56 (d, J = 8.3 Hz, 1H), 4.01 (s, 3H), 3.89 (t, J = 6.9 Hz, 2H), 2.54 (t, J = 8.3 Hz, 2H), 2.06-2.18 (m, 2H); MS m/z: 402 (M + 1).

14.2.w *5-(4-Isopropylpiperazin-1-yl)-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine trihydrochloride*

[0247] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.07 (br s, 1H), 11.61 (br s, 1H), 8.03-8.13 (m, 3H), 7.94-8.01 (m, 2H), 7.40 (d, J = 8.3 Hz, 1H), 3.45-4.00 (m, 5H), 3.48-3.40 (m, 2H), 3.20-3.43 (m, 2H), 1.34 (d, J = 6.3 Hz, 6H); MS m/z: 381 (M + 1).

14.2.x *1-(6-{[6-(5-Methyl-1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)pyrrolidin-2-one dihydrochloride*

[0248] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.84 (br s, 1H), 8.45 (dd, J_1 = 8.8 Hz, J_2 =2.4 Hz, 1H), 7.95-8.00 (m, 3H), 7.74-7.77 (m, 2H), 7.42 (t, J = 8.0 Hz, 1H), 3.90 (t, J = 6.8 Hz, 2H), 2.56 (s, 3H), 2.53 (t, J = 6.8 Hz, 2H), 2.09-2.16 (m, 2H); MS m/z: 352 (M + 1).

14.2.y *N-[6-(5-Isopropyl-1,3-thiazol-2-yl)pyridin-2-yl]-5-(4-methylpiperazin-1-yl)pyridin-2-amine dihydrochloride*

[0249] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.45 (br s, 1H), 8.14 (dd, J_1 = 9.2 Hz, J_2 =2.8 Hz, 1H), 8.07 (d, J = 2.8 Hz, 1H), 7.98 (t, J = 8.4 Hz, 1H), 7.88 (d, J = 9.2 Hz, 1H), 7.76 (d, J = 7.2 Hz, 1H), 7.38 (d, J = 8.4 Hz, 1H), 3.88 (d, J = 11.2 Hz, 2H), 3.52 (d, J = 11.2 Hz, 2H), 3.15-3.37 (m, 5H), 1.39 (d, J = 6.8 Hz, 6H); MS m/z: 395 (M + 1).

14.2.z *5-(1-Methylpiperidin-3-yl)-N-(6-pyrazin-2-ylpyridin-2-yl)pyridin-2-amine trihydrochloride*

[0250] ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.31 (br s, 1H), 10.91 (br s, 1H), 9.60 (d, J = 1.5 Hz, 1H), 8.91 (t, J = 2.4 Hz, 1H), 8.84 (d, J = 2.4 Hz, 1H), 8.44 (d, J = 2.0 Hz, 1H), 8.07-8.22 (m, 3H), 7.74 (d, J = 8.8 Hz, 1H), 7.61 (dd, J_1 = 6.9 Hz, J_2 =2.4 Hz, 1H), 3.40-3.56 (m, 2H), 3.13-3.32 (m, 2H), 2.88-3.00 (m, 1H), 2.77 (s, 1.5H), 2.76 (s, 1.5H), 1.90-2.02 (m, 3H), 1.62-1.74 (m, 1H); MS m/z: 347 (M + 1).

EXAMPLE 15

***Preparation of* 18 *from* 17**

15.1 Stille Cross-Coupling

[0251] A mixture of 1.41 mmol of **17**, 1.41 mmol of **14**, and 0.07 mmol of $Pd(PPh_3)_4$ in 10 mL of toluene was stirred at 100 °C for 15 h under Ar. The reaction was quenched with 10 mL of saturated $NaHCO_3$. After the mixture was extracted with chloroform, the organic phase was washed with saturated NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography to give 1.16 mmol of **18**.

[0252] Most of **18** were converted to HCl salt by adding excess 4 M of HCl in 1,4-dioxane to a solution of **18** in MeOH. The pure salts were obtained by removing the solvents under reduced pressure or crystallizing in ethyl acetate.

15.2 Results

[0253] Analytical data for exemplary compounds of structure **18** are provided below.

15.2.a *4,6-Dipyridin-2-yl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazine*

[0254] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 4.8 Hz, 1H), 8.38 (d, J = 4.8 Hz, 1H), 8.26 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.99 (d, J = 8.4 Hz, 1H), 7.72 (t, J = 7.6 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 7.27 (d, J = 8.4 Hz, 1H), 7.22 (t, J = 4.8 Hz, 1H), 6.93 (t, J = 4.8 Hz, 1H), 4.39 (t, J = 4.4 Hz, 2H), 4.31 (t, J = 4.4 Hz, 2H); MS *m/z*: 291 (M + 1).

15.2.b *(5-Nitro-2,2'-bipyridin-6-yl)(pyridin-2-yl)amine*

[0255] ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.6 (s, 1H), 8.75 (d, J = 4.4 Hz, 1H), 8.70 (d, J = 8.8 Hz, 1H), 8.47 (d, J = 8.0 Hz, 1H), 8.43 (d, J = 4.4 Hz, 1H), 8.35 (d, J = 8.0 Hz, 1H), 8.10 (d, J = 8.8 Hz, 1H), 7.89 (t, J = 8.0 Hz, 1H), 7.81 (t, J_1 = 8.0 Hz, J_2 = 4.4 Hz, 1H); MS *m/z*: 294 (M + 1).

15.2.c *N-[6-(Pyridin-2-ylamino)-2,2'-bipyridin-5-yl]acetamide*

[0256] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68-8.69 (m, 1H), 8.51 (d, J = 8.0 Hz, 1H), 8.47 (d, J = 8.0 Hz, 1H), 8.35 (d, J = 8.0 Hz, 1H), 8.23-8.27 (m, 1H), 7.65-7.80 (m, 4H), 7.30-7.35 (m, 1H), 7.05-7.09 (m, 1H), 2.17 (s, 3H); MS *m/z*: 306 (M + 1).

15.2.d *(5-Methoxy-2,2'-bipyridin-6-yl)(pyridin-2-yl)amine*

[0257] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, J = 8.4 Hz, 1H), 8.62 (m, 1H), 8.27-8.29 (m, 2H), 7.95 (d, J = 8.4 Hz, 2H), 7.80 (m, 1H), 7.74 (m, 1H), 7.24 (dd, J_1 = 8.4 Hz, J_2 = 4.8 Hz, 1H), 7.13 (d, J = 8.4 Hz, 1H), 6.90 (dd, J_1 = 8.4 Hz, J_2 = 4.8 Hz, 1H), 3.94 (s, 3H); MS *m/z*: 279 (M + 1).

15.2.e *Methyl 6-(pyridin-2-ylamino)-2,2'-bipyridine-5-carboxylate*

[0258] ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.39 (br s, 1H), 8.72 (s, 1H), 8.69 (s, 1H), 8.44 (m, 1H), 8.42 (m, 1H), 8.36 (m, 1H), 8.24 (d, J = 8.0 Hz, 1H), 7.83 (t, J = 7.2 Hz, 1H), 7.75 (m, 1H), 7.34 (dd, J_1 = 8.4 Hz, J_2 = 5.2 Hz, 1H), 7.07 (dd, J_1 = 8.4 Hz, J_2 = 5.2 Hz, 1H), 4.33 (s, 3H); MS *m/z*: 307 (M + 1).

15.2.f *N,N-Dimethyl-6-(pyridin-2-ylamino)-2,2'-bipyridine-5-carboxamide*

[0259] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67-8.69 (m, 2H), 8.47 (d, J = 8.0 Hz, 1H), 8.29 (d, J = 4.8 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.85 (t, J = 7.6 Hz, 1H), 7.71 (t, J = 7.6 Hz, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 4.8 Hz, 1H), 6.91 (t, J = 4.8 Hz, 1H), 3.12 (s, 3H), 3.11 (s, 3H); MS *m/z*: 320 (M + 1).

15.2.g 5-Isopropoxy-N-pyridin-2-yl-2,2'-bipyridin-6-amine hydrochloride

[0260] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, J = 8.4 Hz, 1H), 8.61-8.63 (m, 1H), 8.27-8.29 (m, 2H), 7.98 (br s, 1H), 7.94 (d, J = 8.4 Hz, 1H), 7.76 (t, J = 6.8 Hz, 1H), 7.72 (t, J = 6.8 Hz, 1H), 7.17-7.23 (m, 1H), 7.13 (d, J = 8.4 Hz, 1H), 6.88-6.91 (m, 1H), 4.63-4.71 (m, 6H), 1.42 (d, J = 1.6 Hz, 1H), 1.41 (d, J = 1.6 Hz, 1H); MS *m/z*: 307 (M + 1).

15.2.h 5-(Benzyloxy)-N-pyridin-2-yl-2,2'-bipyridin-6-amine

[0261] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.12 (s, 2H), 6.89 (dd, J_1 = 7.6 Hz, J_2 = 4.8 Hz, 1H), 7.17 (d, J = 8.0 Hz, 1H), 7.20 (dd, J_1 = 7.6 Hz, J_2 = 4.8 Hz, 1H), 7.34-7.44 (m, 5H), 7.70-7.78 (m, 2H), 7.92 (d, J = 8.0 Hz, 1H), 7.97 (br s, 1H), 8.24-8.28 (m, 2H), 8.61 (d, J = 4.8 Hz, 1H), 8.68 (d, J = 7.6 Hz, 1H); MS *m/z*: 355 (M + 1).

15.2.i 5-(2-Methoxyethoxy)-N-pyridin-2-yl-2,2'-bipyridin-6-amine

[0262] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, J = 8.0 Hz, 1H), 8.62-8.64 (m, 1H), 8.27-8.29 (m, 2H), 8.02 (br s, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.80 (t, J = 7.6 Hz, 1H), 7.73 (t, J = 7.6 Hz, 1H), 7.23 (t, J = 5.2 Hz, 1H), 7.17 (d, J = 8.0 Hz, 1H), 6.91 (t, J = 5.2 Hz, 1H), 4.25 (t, J = 4.8 Hz, 2H), 3.81 (t, J = 4.8 Hz, 2H), 3.46 (s, 3H); MS *m/z*: 323 (M + 1).

15.2.j Methyl {[6-(pyridin-2-ylamino)-2,2'-bipyridin-5-yl]oxy}acetate

[0263] ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (br s, 1H), 8.62 (d, J = 4.8 Hz, 1H), 8.31-8.33 (m, 2H), 8.28 (d, J = 7.6 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.78 (t, J = 7.6 Hz, 1H), 7.73 (t, J = 7.6 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.25 (t, J = 4.8 Hz, 1H), 7.09 (t, J = 4.8 Hz, 1H), 4.71 (s, 2H), 4.18 (s, 3H); MS *m/z*: 337 (M + 1).

EXAMPLE 16

***Preparation of* 18**

16.1 Stannylation

[0264] **17** (5 mmol, in 50 mL of dry THF) was added, through a canular, to a suspension of 6 mmol of KH (30% mineral oil) in 50 mL of dry THF at 0 °C under N_2. The resulting mixture was stirred for 30 min at 0 °C and then cooled to -78 °C. To the cold solution was added 10.5 mmol of n-BuLi (2.5 M in hexane), and the mixture was stirred for 1 h before 10.5 mmol of Bu_3SnCl was added. The solution then was stirred for 2 h at -78 °C and allowed to warm to rt over 4 h before the reaction was quenched with 5 mL of isopropanol and 50 mL of water. After the mixture was diluted with 200 mL of ethyl acetate, the organic

phase of the mixture was washed with saturated NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography to give 4.4 mmol of **19**.

16.2 Results

[0265] Analytical data for exemplary compounds of structure **19** are provided below.

16.2.a (5-Chloro-pyridin-2-yl)-(6-tributylstannanyl-pyridin-2-yl)-amine

[0266] ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.71 (s, 1H), 8.18 (d, J = 2.6 Hz, 1H), 8.10 (d, J = 9.0 Hz, 1H), 7.62-7.58 (m, 1H), 7.43 (t, J = 8.2 Hz, 1H), 7.28 (d, J = 8.4 Hz, 1H), 6.90 (d, J = 6.8 Hz, 1H), 1.62-1.45 (m, 6H), 1.42-1.19 (m, 6H), 1.17-0.94 (m, 6H), 0.91-0.72 (m, 9H); MS *m/z*: 496 (M + 1).

16.2.b (5-Phenyl-pyridin-2-yl)-(6-tributylstannanyl-pyridin-2-yl)-amine

[0267] ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.66 (s, 1H), 8.52 (d, J = 2.4 Hz, 1H), 8.13 (d, J = 8.9 Hz, 1H), 7.87 (dd, J_1 = 8.7 Hz, J_2 = 2.5 Hz, 1H), 7.65-7.62 (m, 2H), 7.47-7.39 (m, 4H), 7.31 (d, J = 7.3 Hz, 1H), 6.91 (d, J = 6.5 Hz, 1H), 1.69-1.48 (m, 6H), 1.34-1.17 (m, 6H), 1.14-1.00 (m, 6H), 0.97-0.74 (m, 9H); MS *m/z*: 538 (M + 1).

16.3 Synthesis of **18** *from* **19**

[0268] A solution of 0.25 mmol of **19**, 0.275 mmol of **12**, and 0.025 mmol of $Pd(PPh_3)_4$ in 4 mL of dry DMF was refluxed for 1 day under N_2. The reaction was quenched with 2 mL of concentrated NH_4OH. After removal of DMF under reduced pressure, the residue was diluted with 100 mL of ethyl acetate and the organic mixture was washed with saturated NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography to give 0.12 mmol of **18**.

[0269] Most of **18** were converted to HCl salt by adding excess 4 M of HCl in 1,4-dioxane to a solution of **18** in MeOH. The pure salts were obtained by removing the solvents under reduced pressure or crystallizing in ethyl acetate.

16.4 Results

[0270] Analytical data for exemplary compounds of structure **18** are provided below.

16.4.a (5-Chloro-pyridin-2-yl)-[6-(1-methyl-1H-imidazol-4-yl)-pyridin-2-yl]-amine · 2HCl

[0271] ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.65 (s, 1H), 8.99 (s, 1H), 8.33 (d, J = 2.4 Hz, 1H), 8.23 (d, J = 1.3 Hz, 1H), 7.99 (d, J = 8.9 Hz, 1H), 7.91 (d, J = 8.7 Hz, 1H), 7.86 (dd, J_1 =

6.2 Hz, J_2 = 4.3 Hz, 1H), 7.52 (d, J = 7.5 Hz, 1H), 7.39 (d, J = 8.5 Hz, 1H), 3.90 (s, 3H); MS *m/z*: 286 (M + 1).

16.4.b (5-Chloro-pyridin-2-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine · 2HCl

[0272] ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.71 (s, 1H), 9.53 (s, 1H), 8.80 (d, J = 1.5 Hz, 1H), 8.75 (d, J = 2.5 Hz, 1H), 8.39 (d, J = 2.1 Hz, 1H), 7.98-7.94 (m, 2H), 7.93 (d, J = 9.0 Hz, 1H), 7.85 (d, J = 9.0 Hz, 1H), 7.60 (dd, J_1 = 6.4 Hz, J_2 = 2.9 Hz, 1H); MS *m/z*: 284 (M + 1).

16.4.c (5-Phenyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine · 2HCl

[0273] ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.10 (s, 1H), 8.78 (d, J = 1.8 Hz, 1H), 8.49 (dd, J_1 = 6.4 Hz, J_2 = 2.9 Hz, 1H); 8.05-7.97 (m, 4H), 7.83 (d, J = 7.5 Hz, 1H), 7.78 (d, J = 7.2 Hz, 2H), 7.55-7.40 (m, 4H); MS *m/z*: 331 (M + 1).

EXAMPLE 17

***Preparation of* 22**

17.1 Synthesis of **21**

[0274] To a solution of 25 mmol of **20** in 80 mL of dry THF at 0 °C was added 25 mmol of KH (30% mineral oil) under N_2. The suspension was stirred for 20 min before 10 mmol of **15** in 20 mL of dry THF was added over a period of 10 min. The resulting mixture was stirred for two days at 60 °C under N_2. The reaction was quenched dropwise with isopropanol (10 mL) and saturated NaCl (50 mL) at 0 °C and the mixture was diluted with 200 mL of ethyl acetate. After separating the two phases, the organic phase was washed with saturated NaCl, dried over $MgSO_4$, and concentrated under reduced pressure to give 10 mmol of **21**.

17.2 Results

[0275] Analytical data for exemplary compounds of structure **21** are provided below.

17.2.a 2,6-Di-pyrazol-1-yl-pyridine

[0276] ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.92 (d, J = 2.1 Hz, 2H), 8.11 (t, J = 7.8 Hz, 1H), 7.84 (d, J = 0.9 Hz, 2H), 7.79 (d, J = 8.0 Hz, 2H), 6.61 (dd, J_1 = 2.8 Hz, J_2 = 0.9 Hz, 2H); MS *m/z*: 212 (M + 1).

17.2.b 2,6-Bis-(4-methyl-pyrazol-1-yl)-pyridine

[0277] ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.67 (s, 2H), 8.04 (t, J = 8.0 Hz, 1H), 7.69 (s, 2H), 7.66 (d, J = 3.6 Hz, 2H), 2.12 (s, 6H); MS *m/z*: 240 (M + 1).

17.3 Synthesis of **22** *via Nucleophilic Replacement*

[0278] To a solution of 1.66 mmol of **11** in 10 mL of anhydrous 1,4-dioxane was added 6.6 mmol of NaH (60% in mineral oil) followed by the addition of 1.66 mmol of **21**, and the resulting mixture was stirred at 100 °C overnight under N_2. After the reaction was quenched with methanol, the solvents were removed. The residue was dissolved in 40 mL of ethyl acetate and the organic solution was washed with saturated NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography to give 0.8 mmol of **22**.

17.4 Results

[0279] Analytical data for exemplary compounds of structure **22** are provided below.

17.4.a (5-Methoxy-pyridin-2-yl)-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine · 2HCl

[0280] ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.61 (s, 1H), 8.40 (s, 1H), 8.12 (d, J = 3.0 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.89 (dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 1H), 7.77 (dd, J_1 = 5.7 Hz, J_2 = 3.5 Hz, 1H), 7.65 (s, 1H), 7.46 (d, J = 7.9 Hz, 1H), 7.18 (d, J = 8.0 Hz, 1H), 3.86 (s, 3H), 2.14 (s, 3H); MS *m/z*: 282 (M + 1).

17.4.b [6-(4-Methyl-pyrazol-1-yl)-pyridin-2-yl]-(5-morpholin-4-yl-pyridin-2-yl)-amine · 2HCl

[0281] ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.34 (s, 1H), 8.44 (s, 1H), 8.21 (dd, J_1 = 9.6 Hz, J_2 = 2.6 Hz, 1H), 7.96 (s, 1H), 8.04-7.92 (m, 1H), 7.50 (dd, J_1 = 9.6 Hz, J_2 = 3.7 Hz, 1H), 7.66 (s, 1H), 7.52 (d, J = 4.0 Hz, 1H), 7.14 (d, J = 8.2 Hz, 1H), 2.06 (s, 3H), 3.78-3.68 (m, 4H), 3.18-3.14 (m, 4H); MS *m/z*: 337 (M + 1).

17.4.c [5-(3-Fluoro-phenyl)-pyridin-2-yl]-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine · 2HCl

[0282] ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.99 (s, 1H), 8.78 (s, 1H), 8.50 (d, J = 9.2 Hz, 1H), 8.45 (s, 1H), 7.96 (t, J = 8.0 Hz, 1H), 7.89 (d, J = 8.8 Hz, 1H), 7.67 (s, 1H), 7.62 (d, J = 9.3 Hz, 1H), 7.59-7.52 (m, 3H), 7.32 (d, J = 8.0 Hz, 1H), 7.26 (t, J = 8.2 Hz, 1H), 2.15 (s, 3H); MS *m/z*: 346 (M + 1).

EXAMPLE 18

***Preparation of* 22**

18.1 Synthesis of **23**

[0283] A mixture of 3.18 mmol of **15**, 3.50 mmol of pyrazole **20**, 0.32 mmol of $Pd_2(dba)_3$, 0.32 mmol of BINAP, and 4.77 mmol of Cs_2CO_3 in 30 mL of toluene was stirred at 80°C for one day under Ar. The reaction mixture was diluted with 100 mL of chloroform and the organic solution was washed with saturated NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography to give 1.36 mmol of **23**.

18.2 Results

[0284] Analytical data for exemplary compounds of structure **23** are provided below.

18.2.a *6-Iodo-3-methoxy-2-(1H-pyrazol-1-yl)pyridine*

[0285] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 2.0 Hz, 1H), 7.63 (d, J = 8.8 Hz, 1H), 7.61 (d, J = 2.0 Hz, 1H), 7.08 (d, J = 8.8 Hz, 1H), 6.45 (t, J = 2.0 Hz, 1H), 3.90 (s, 3H); MS *m/z*: 302 (M + 1).

18.2.b *2-Bromo-6-(4-bromo-1H-pyrazol-1-yl)pyridine*

[0286] ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (s, 1H), 7.88 (d, J= 8.0 Hz, 1H), 7.64-7.70 (m, 2H), 7.38 (d, J=8.0 Hz, 1H); MS *m/z*: 306 (M + 1).

18.3 Synthesis of **22** *via Nucleophilic Replacement*

[0287] To a solution of 1.66 mmol of **11** in 10 mL of anhydrous 1,4-dioxane was added 6.6 mmol of NaH (60% in mineral oil) followed by the addition of 1.66 mmol of **23**, and the resulting mixture was stirred at 100 °C overnight under N_2. After the reaction was quenched with methanol, the solvents were removed. The residue was dissolved in 40 mL of ethyl acetate and the organic solution was washed with saturated NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography to give 0.8 mmol of **22**.

18.4 Results

[0288] Analytical data for exemplary compounds of structure **22** are provided below.

18.4.a 5-Methyl-N-[6-(1H-pyrazol-1-yl)pyridin-2-yl]pyridin-2-amine

[0289] ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.75 (s, 1H), 8.52 (d, J= 3.0 Hz, 1H), 8.10 (s, 1H), 7.77-7.81 (m, 2H), 7.72 (d, J= 8.3 Hz, 1H), 7.58 (dd, J_1 = 8.3 Hz, J_2 = 1.9 Hz, 1H), 7.52 (d, J= 8.3 Hz, 1H), 7.33 (d, J= 7.9 Hz, 1H), 6.58 (br t, J= 1.9 Hz, 1H), 2.24 (s, 3H); MS *m/z*: 252 (M + 1).

18.4.b Methyl 6-{[6-(1H-pyrazol-1-yl)pyridin-2-yl]amino}nicotinate monohydrochloride

[0290] ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.54 (s, 1H), 8.82 (d, J= 2.4 Hz, 1H), 8.59 (d, J= 2.4 Hz, 1H), 8.26 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1H), 7.92 (d, J= 9.3 Hz, 1H), 7.90 (t, J = 8.3 Hz, 1H), 7.82 (s, 1H), 7.60 (d, J= 7.9 Hz, 1H), 7.49 (d, J= 7.8 Hz, 1H), 6.60 (br t, J= 1.5 Hz, 1H), 3.85 (s, 3H); MS *m/z*: 296 (M + 1).

18.4.c 5-Methoxy-N-(5-morpholin-4-ylpyridin-2-yl)-6-(1H-pyrazol-1-yl)pyridin-2-amine dihydrochloride

[0291] ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.48 (s, 1H), 8.59 (d, J = 2.8 Hz, 1H), 8.19 (dd, J_1 = 9.6 Hz, J_2 = 2.8 Hz, 1H), 7.98 (d, J = 8.8 Hz, 1H), 7.94 (d, J = 2.4 Hz, 1H), 7.77 (d, J = 2.4 Hz, 1H), 7.60 (d, J = 9.6 Hz, 1H), 7.28 (d, J = 8.8 Hz, 1H), 6.63 (t, J = 2.4 Hz, 1H), 3.98 (s, 3H), 3.77 (t, J = 4.8 Hz, 4H), 3.18 (t, J = 4.8 Hz, 4H); MS *m/z*: 353 (M + 1).

18.4.d 4-Methyl-1-(6-{[6-(4-methyl-1H-pyrazol-1-yl)pyridin-2-yl]amino}pyridin-3-yl)piperazin-2-one dihydrochloride

[0292] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.50-12.00 (br, 1H), 10.05-10.40 (br, 1H), 8.35 (s, 1H), 8.25-8.31 (m, 1H), 7.94 (d, J= 8.7 Hz, 1H), 7.76-7.88 (m, 2H), 7.63 (s, 1H), 7.33-7.45 (m, 2H), 3.45-4.35 (m, 6H), 2.93 (s, 3H), 2.14 (s, 3H); MS *m/z*: 364 (M + 1).

18.4.e 4-Methyl-1-(6-{[6-(1H-pyrazol-1-yl)pyridin-2-yl]amino}pyridin-3-yl)piperazin-2-one dihydrochloride

[0293] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.70-12.15 (br, 1H), 10.30-10.60 (br, 1H), 8.57-8.62 (m, 1H), 8.28-8.34 (m, 1H), 7.80-7.94 (m, 4H), 7.42-7.50 (m, 2H), 6.57-6.62 (m, 1H), 3.95-4.50 (m, 3H), 3.70-3.95 (m, 2H), 3.50-3.70 (m, 1H), 2.92 (s, 3H); MS *m/z*: 350 (M + 1).

18.4.f 1-(6-{[6-(4-Bromo-1H-pyrazol-1-yl)pyridin-2-yl]amino}pyridin-3-yl)-4-methylpiperazin-2-one dihydrochloride

[0294] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.50-11.90 (br, 1H), 10.31 (s, 1H), 8.70 (s, 1H), 8.28 (d, J = 2.4 Hz, 1H), 7.96 (s, 1H), 7.94 (d, J = 9.3 Hz, 1H), 7.88 (dd, J_1 = 8.3 Hz, J_2 = 7.8 Hz, 1H), 7.83 (dd, J_1 = 9.3 Hz, J_2 = 2.4 Hz 1H), 7.49 (d, J = 7.8 Hz, 1H), 7.40 (d, J = 7.8 Hz, 1H), 3.70-4.23 (m, 6H), 2.93 (s, 3H); MS *m/z*: 430 (M + 1).

EXAMPLE 19

***Preparation of* 24**

19.1 Reduction

[0295] To a solution of 2.2 mmol of $LiAlH_4$ in 4 mL of ether was added 0.74 mmol of **18** at 0 °C and stirred for 1 h. The reaction mixture was quenched with saturated Na_2SO_4, filtered through Celite, and washed with THF. The filtrate was dried over $MgSO_4$ and concentrated. The residue was purified by column chromatography on silica gel to give 0.25 mmol of **24**.

19.2 Results

[0296] Analytical data for exemplary compounds of structure **24** are provided below.

19.2.a (6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methanol

[0297] ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.86 (s, 1H), 8.21 (d, J = 1.9 Hz, 1H), 8.00 (d, J = 8.3 Hz, 1H), 7.98 (d, J = 2.9 Hz, 1H), 7.85 (d, J = 3.4 Hz, 1H), 7.80 (t, J = 7.8 Hz, 1H), 7.70 (dd, J_1 = 8.6 Hz, J_2 = 2.2 Hz, 1H), 7.62 (s, 1H), 7.60 (s, 1H), 5.15 (t, J = 5.8 Hz, 1H), 4.46 (d, J = 5.8 Hz, 2H); MS *m/z*: 285 (M + 1).

19.2.b 3-(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)propan-1-ol dihydrochloride

[0298] ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.58 (s, 1H), 8.38 (s, 1H), 8.23 (dd, J = 2.2 Hz, 8.8 Hz, 1H), 8.04-8.08 (m, 2H), 8.01 (d, J = 3.5 Hz, 1H), 7.89 (d, J = 7.3 Hz, 1H), 7.83 (d, J = 8.8 Hz, 1H), 7.44 (d, J = 7.8 Hz, 1H), 4.82 (br, 1H), 3.44 (t, J = 6.3 Hz, 2H); MS *m/z*: 313 (M + 1).

EXAMPLE 20

***Preparation of* 25**

20.1 Halogenation

[0299] A suspension of 10.1 mmol of **24** in 15 mL of $SOCl_2$ was stirred at rt for 30 min. The reaction mixture was concentrated in vacuo and the residue was diluted EtOH-AcOEt and preciptates were collected by filtration to give 6.5 mmol of **25**.

20.2 Results

[0300] Analytical data for exemplary compound of structure **25** is provided below.

20.2.a *5-(Chloromethyl)-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine dihydrochloride*

[0301] ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.49 (br s, 1H), 8.47 (s, 1H), 8.18-7.89 (m, 5H), 7.91 (d, J = 7.7 Hz, 1H), 7.55 (d, J = 8.3 Hz, 1H), 4.85 (s, 2H); MS *m/z*: 304 (M + 1).

EXAMPLE 21

***Preparation of* 26**

21.1 Nucleophilic Replacement

[0302] A solution of 0.61 mmol of **25** in 5 mL of DMF was added 3.0 mmol of a primary or secondary amine at rt and stirred for 20 min. The reaction mixture was concentrated *in vacuo* and the residue was diluted with AcOEt and water. The mixture was extracted with diluted HCl and the aqueous phase was made alkaline with K_2CO_3. The mixture was extracted with AcOEt and the organic phase was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified with column chromatography on silica gel and converted into HCl salt to give 0.47 mmol of **26**.

21.2 Results

[0303] Analytical data for exemplary compound of structure **26** are provided below.

21.1.a *5-(Pyrrolidin-1-ylmethyl)-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine trihydrochloride*

[0304] ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 11.78 (br s, 1H), 9.36 (d, J = 1.9 Hz, 1H), 9.30 (br, 1H), 8.43 (dd, J_1 = 8.8 Hz, J_2 = 1.9 Hz, 1H), 7.96-8.08 (m, 4H), 7.86 (d, J =

7.3 Hz, 1H), 7.59 (d, J = 8.3 Hz, 1H), 4.42 (d, J = 5.3 Hz, 2H), 3.35-3.47 (m, 2H), 3.02-3.15 (m, 2H), 1.84-2.10 (m, 2H); MS *m/z*: 338 (M + 1).

21.2.b *5-(2-Pyrrolidin-1-ylethyl)-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine trihydrochloride*

[0305] ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.74 (s, 1H), 8.49 (d, J = 2.4 Hz, 1H), 8.28 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1H), 8.06-8.09 (m, 2H), 8.02 (d, J = 2.8 Hz, 1H), 7.91 (t, J = 8.8 Hz, 2H), 7.49 (d, J = 7.6 Hz, 1H), 3.53 (m, 2H), 3.45 (m, 2H), 3.16 (t, J = 6.4 Hz, 2H), 3.06 (m, 2H), 2.03 (m, 2H), 1.92 (m, 2H); MS *m/z*: 352 (M + 1).

21.2.c *5-[(Benzylamino)methyl]-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine dihydrochloride*

[0306] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.28 (s, 1H), 9.93 (s, 1H), 8.53 (d, J = 2.0 Hz, 1H), 8.24 (d, J = 9.2 Hz, 1H), 8.23 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 1H), 8.07 (d, J = 3.4 Hz, 1H), 7.94-7.97 (m, 2H), 7.79 (d, J = 7.3 Hz, 1H), 7.56-7.63 (m, 2H), 7.40-7.48 (m, 2H), 4.16-4.23 (m, 4H); MS *m/z*: 374 (M + 1).

21.2.d *5-[(Cyclohexylamino)methyl]-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine dihydrochloride*

[0307] ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.42 (br s, 1H), 8.55 (d, J = 1.9 Hz, 1H), 8.23 (d, J = 8.8 Hz, 1H), 7.99-8.05 (m, 2H), 7.90-7.96 (m, 2H), 7.77 (d, J = 7.3 Hz, 1H), 7.58 (d, J = 8.3 Hz, 1H), 4.10-4.21 (m, 2H), 2.94-3.07 (m, 1H), 2.15 (d, J = 9.8 Hz, 2H), 11.07 (br s, 1H), 1.79 (br d, J = 11.7 Hz, 2H), 1.56-1.65 (m, 1H), 1.35-1.49 (m, 2H), 1.03-1.32 (m, 3H); MS *m/z*: 366 (M + 1).

21.2.e *5-[(Isopropylamino)methyl]-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine trihydrochloride*

[0308] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.76 (br s, 1H), 9.57 (br s, 1H), 8.63 (d, J = 2.4 Hz, 1H), 8.37 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1H), 8.05 (d, J = 2.8 Hz, 1H), 7.96-8.02 (m, 3H), 7.83 (d, J = 6.8 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 4.18 (t, J = 6.0 Hz, 2H), 3.29-3.35 (m, 1H), 1.34 (d, J = 6.4 Hz, 6H); MS *m/z*: 326 (M + 1).

21.2.f *5-{[Cyclohexyl(methyl)amino]methyl}-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine trihydrochloride*

[0309] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.04 (br s, 1H), 8.64 (d, J = 2.0 Hz, 1H), 8.35 (dd, J_1 = 8.8 Hz, J_2 = 2.0 Hz, 1H), 8.04 (d, J = 2.8 Hz, 1H), 7.98-8.01 (m, 2H), 7.97 (d, J = 2.8 Hz, 1H), 7.81 (d, J = 7.6 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 4.41-4.45 (m, 1H), 4.21-4.26 (m,

1H), 3.20 (t, J = 11.6 Hz, 1H), 2.59 (d, J = 4.8 Hz, 3H), 2.19 (t, J = 11.6 Hz, 2H), 1.84 (t, J = 11.6 Hz, 2H), 1.12-1.63 (m, 6H); MS *m/z*: 380 (M + 1).

21.2.g *5-[(tert-Butylamino)methyl]-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine dihydrochloride*

[0310] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.58 (br s, 1H), 9.51 (br s, 1H), 8.63 (br s, 1H), 8.36 (t, J = 8.4 Hz, 1H), 8.03 (d, J = 3.2 Hz, 1H), 7.94-8.00 (m, 3H), 7.80 (dd, J_1 = 7.6 Hz, J_2 = 3.2 Hz, 1H), 7.52 (d, J = 8.4 Hz, 1H), 4.14 (br s, 2H), 1.40 (s, 9H); MS *m/z*: 340 (M + 1).

21.2.h *5-[(Cyclopentylamino)methyl]-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine trihydrochloride*

[0311] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.83 (br s, 1H), 9.72 (br s, 1H), 8.63 (br s, 1H), 8.37 (d, J = 9.2 Hz, 1H), 8.05 (d, J = 3.2 Hz, 1H), 7.96-8.03 (m, 3H), 7.83 (d, J = 7.2 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 4.18 (t, J = 5.6 Hz, 2H), 3.44-3.54 (m, 1H), 1.94-2.04 (m, 2H), 1.70-1.83 (m, 4H), 1.49-1.59 (m, 2H); MS *m/z*: 352 (M + 1).

21.2.i *5-(3,4-Dihydroisoquinolin-2(1H)-ylmethyl)-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine dihydrochloride*

[0312] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.85 (br s, 1H), 8.43 (s, 1H), 8.32 (d, J = 8.8 Hz, 1H), 7.79-8.10 (m, 9H), 7.63 (d, J = 8.4 Hz, 1H), 4.58 (s, 2H), 4.36 (s, 2H), 3.94 (t, J = 8.0 Hz, 2H), 3.16 (t, J = 8.0 Hz, 2H); MS *m/z*: 400 (M + 1).

21.2.j *5-[(2,6-Dimethylpiperidin-1-yl)methyl]-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine trihydrochloride*

[0313] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.58 (br s, 1H), 8.56 (s, 1H), 8.33 (d, J = 8.8 Hz, 1H), 8.04 (d, J = 3.2 Hz, 1H), 7.97-8.00 (m, 3H), 7.81 (d, J = 7.6 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 4.49 (s, 2H), 3.01-3.10 (m, 2H), 1.70-1.83 (m, 6H), 1.58 (d, J = 6.0 Hz, 6H); MS *m/z*: 380 (M + 1).

21.2.k *5-[(Diethylamino)methyl]-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine dihydrochloride*

[0314] ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.88 (br s, 1H), 10.82 (br s, 1H), 8.54 (s, 1H), 8.19 (d, 1H), 8.02-8.06 (m, 2H), 7.90-7.94 (m, 2H), 7.75 (d, 1H), 7.64 (d, 1H), 4.30 (d, 2H), 3.07 (m, 4H), 1.28 (s, 6H); MS *m/z*: 340 (M + 1).

21.2.l *5-(Piperidin-1-ylmethyl)-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine dihydrochloride*

[0315] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.17 (br s, 1H), 11.06 (br s, 1H), 8.55 (q, 1H), 8.23 (q, 1H), 8.02-8.04 (m, 2H), 7.93-7.97 (m, 2H), 7.78 (d, 1H), 7.63 (d, 1H), 4.28 (d, 2H),

3.34 (d, 2H), 2.84-2.89 (m, 2H), 1.80-1.92 (m, 4h), 1.69-1.72 (m, 1H), 1.35-1.41 (m, 1H); MS *m/z*: 352 (M + 1).

21.2.m *5-(Morpholin-4-ylmethyl)-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine dihydrochloride*

[0316] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.75 (br s, 1H), 10.99 (br s, 1H), 8.53 (d, 1H), 8.20 (d, 1H), 8.02-8.05 (m, 2H), 7.91-7.95 (m, 2H), 7.76 (d, 1H), 7.64 (d, 1H), 4.35 (br s, 2H), 3.94-3.97 (m, 2H), 3.81-3.87 (m, 2H), 3.28-3.31 (m, 2H), 3.08-3.11 (m, 2H); MS *m/z*: 354 (M + 1).

21.2.n *5-(3,6-Dihydropyridin-1(2H)-ylmethyl)-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine dihydrochloride*

[0317] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.31 (br s, 1H), 11.11 (br s, 1H), 8.57 (d, 1H), 8.24 (q, 1H), 8.03-8.07 (m, 2H), 7.92-7.96 (m, 2H), 7.77 (d, 1H), 7.63 (d, 1H), 5.90-5.92 (m, 1H), 5.70 (d, 1H), 4.32-4.42 (m, 2H), 3.61 (br s, 2H), 3.45-3.50 (m, 1H), 3.06-3.09 (m, 1H), 2.50-2.55 (m, 1H), 2.28-2.33 (br d, 1H); MS *m/z*: 350 (M + 1).

21.2.o *5-(1,3-Dihydro-2H-isoindol-2-ylmethyl)-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine dihydrochloride*

[0318] ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.58 (br s, 1H), 11.35 (br s, 1H), 8.67 (s, 1H), 8.36 (d, 1H), 8.03-8.05 (m, 2H), 7.95-7.99 (m, 2H), 7.80 (d, 1H), 7.64 (d, 1H), 7.35-7.41 (m, 4H), 4.65 (br s, 6H); MS *m/z*: 386 (M + 1).

21.2.p *N-[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]pyrazin-2-amine dihydrochloride*

[0319] ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.32 (br s, 1H), 8.44 (s, 1H), 8.25 (d, 1H), 8.15 (s, 1H), 7.99-8.07 (m, 4H), 7.83-7.89 (m, 2H), 7.78 (d, 1H), 7.45 (d, 1H), 4.58 (s, 2H); MS *m/z*: 362 (M + 1).

21.2.q *N-[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]pyrimidin-2-amine dihydrochloride*

[0320] ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.25 (br s, 1H), 8.48 (d, 2H), 8.43 (s, 1H), 8.24 (d, 1H), 7.98-8.06 (m, 3H), 7.86-7.89 (m, 2H), 7.47 (d, 1H), 6.81-6.84 (m, 1H), 4.64 (s, 2H); MS *m/z*: 362 (M + 1).

21.2.r *5-[(Ethylamino)methyl]-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine dihydrochloride*

[0321] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.09 (br s, 1H), 9.46 (br s, 2H), 8.52 (s, 1H), 8.20 (d, J = 8.3 Hz, 1H), 7.92-8.04 (m, 1H), 7.77 (d, J = 7.8 Hz, 1H), 7.60 (d, J = 8.3 Hz, 1H), 2.98-3.20 (m, 2H), (br, 2H), 1.26 (t, J = 7.3 Hz, 3H); MS *m/z*: 312 (M + 1).

21.2.s *5-[(4-Phenyl-3,6-dihydropyridin-1(2H)-yl)methyl]-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine dihydrochloride*

[0322] ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.41 (br s, 1H), 11.11 (br s, 1H), 8.69 (s, 1H), 8.27 (d, J = 8.6 Hz, 1H), 7.91-8.15 (m, 4H), 7.77 (d, J = 7.5 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.30-7.50 (m, 5H), 6.18 (s, 1H), 4.40-4.52 (m, 2H), 3.82 (s, 2H), 3.55-3.65 (m, 1H), 3.20-3.30 (m, 1H), 2.70-3.02 (m, 2H); MS *m/z*: 426 (M + 1).

EXAMPLE 22

***Preparation of* 27**

22.1 Synthesis

[0323] A solution of 0.57 mmol of **18** in 5 mL of formic acid was stirred at 100 °C for 10 h. After the solvents were removed, the residue was dissolved in 10 mL of chloroform and the organic solution was washed with saturated $NaHCO_3$, saturated NaCl, dried over $MgSO_4$, and concentrated under a reduced pressure. The crude product was purified by column chromatography on silica gel to give 0.29 mmol of **27**.

22.2 Results

[0324] Analytical data for exemplary compound of structure **27** is provided below.

22.2.a *3,5-Dipyridin-2-yl-3H-imidazo[4,5-b]pyridine*

[0325] ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 8.98 (d, J = 8.8 Hz, 1H), 8.72 (d, J = 4.0 Hz, 1H), 8.53-7.55 (m, 2H), 8.49 (d, J = 7.6 Hz, 1H), 8.24 (d, J = 8.8 Hz, 1H), 8.00 (t, J = 7.6 Hz, 1H), 7.86 (t, J = 7.6 Hz, 1H), 7.31-7.34 (m, 2H); MS *m/z*: 372 (M + 1).

EXAMPLE 23

***Preparation of the metal complex* 28**

23.1 Synthesis

[0326] To a solution of 0.2 mmol of **18** in EtOH at 60 °C was added 0.1 mL of 1.0 M $FeClO_4$ in ether and a white precipitate forms immediately. To the mixture was added 0.06 mL of triethyl amine and the resulting mixture was stirred for 20 min. After the mixture was cooled to rt, the white precipitate was filtered to yield 60% of **28**.

23.2 Results

[0327] Analytical data for exemplary compounds of structure **28** are provided below.

23.2.a {[2,2']Bipyridinyl-6-yl-pyridin-2-yl-amine}$_2$Fe (II) complex

[0328] MS *m/z*: 551 (M + 1).

EXAMPLE 24

24.1 Assay for Compound Activity Towards hSK Channels

[0329] Cells expressing small conductance, calcium activated potassium channels, such as SK-like channels were loaded with $^{86}Rb^+$ by culture in media containing $^{86}RbCl$. Following loading, the culture media was removed and the cells were washed in EBSS to remove residual traces of $^{86}Rb^+$. Cells were preincubated with the drug (0.01-30 μM in EBSS)and then $^{86}Rb^+$ efflux was stimulated by exposing cells to EBSS solution supplemented with a calcium ionophore, such as ionomycin, in the continued presence of the drug. After a suitable efflux period, the EBSS/ionophore solution was removed from the cells and the $^{86}Rb^+$ content was determined by Cherenkov counting (Wallac Trilux). Cells were then lysed with a SDS solution and the $^{86}Rb^+$ content of the lysate was determined. Percent $^{86}Rb^+$ efflux was calculated according to the following equation:

($^{86}Rb^+$ content in EBSS/($^{86}Rb^+$ content in EBSS + $^{86}Rb^+$ content of the lysate)) x 100

24.2 Results

[0330] Compounds tested in this assay, along with their hSK2 inhibitory activity, are provided in Table 1.

Table 1

Compound Name	hSK2 Inhibitory Activity
(5-Methyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	++++
(5-Fluoro-pyridin-2-yl)-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine	++++
(5-Fluoro-pyridin-2-yl)-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine	++++
(5-Isopropenyl-pyridin-2-yl)-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine	++++
(5-Methoxy-pyridin-2-yl)-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine	++++
(5-Furan-2-yl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	++++
(5-Bromo-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	++++
(5,6,7,8-Tetrahydro-isoquinolin-3-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	++++
(3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-(5-morpholin-4-yl-pyridin-2-yl)-amine	++++
(5-Ethyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	++++
[6-(5-Chloro-thiazol-2-yl)-pyridin-2-yl]-pyridin-2-yl-amine	++++
(3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-(5-pyrrolidin-1-yl-pyridin-2-yl)-amine	++++
1-[6-(3-Methoxy-6-thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-pyrrolidin-2-one	++++
[6-(5-Methyl-thiazol-2-yl)-pyridin-2-yl]-pyridin-2-yl-amine	++++
[6-(5-Chloro-thiazol-2-yl)-pyridin-2-yl]-(5-pyrrolidin-1-yl-pyridin-2-yl)-amine	++++
1-{6-[6-(5-Chloro-thiazol-2-yl)-pyridin-2-ylamino]-pyridin-3-yl}-pyrrolidin-2-one	++++
N^2-[6-(5-Chloro-thiazol-2-yl)-3-methoxy-pyridin-2-yl]-N^5-(2-methoxy-ethyl)-N^5-methyl-pyridine-2,5-diamine	++++
[5-(3,4-Dihydro-1H-isoquinolin-2-ylmethyl)-pyridin-2-yl]-(6-thiazol-2-yl-pyridin-2-yl)-amine	++++
(6-Thiazol-2-yl-pyridin-2-yl)-(5-thiophen-3-yl-pyridin-2-yl)-amine	+++
[5-(5-Methyl-furan-2-yl)-pyridin-2-yl]-(6-thiazol-2-yl-pyridin-2-yl)-amine	+++
(5-Bromo-pyridin-2-yl)-(6-pyrazol-1-yl-pyridin-2-yl)-amine	+++
(5-Bromo-pyridin-2-yl)-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine	+++
(5-Chloro-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	+++

(5-Chloro-pyridin-2-yl)-(6-pyrazol-1-yl-pyridin-2-yl)-amine	+++
(5-Isopropyl-pyridin-2-yl)-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine	+++
[5-(3-Fluoro-phenyl)-pyridin-2-yl]-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine	+++
[5-(2-Methoxy-phenyl)-pyridin-2-yl]-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine	+++
(5-Phenyl-2H-pyrazol-3-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	+++
[3,3']Bipyridinyl-6-yl-(6-pyrazin-2-yl-pyridin-2-yl)-amine	+++
(5-Furan-2-yl-pyridin-2-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine	+++
Isoquinolin-3-yl-(6-thiazol-2-yl-pyridin-2-yl)-amine	+++
(3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-[5-(4-methyl-piperazin-1-yl)-pyridin-2-yl]-amine	+++
(3-Methoxy-6-pyrazin-2-yl-pyridin-2-yl)-[5-(4-methyl-piperazin-1-yl)-pyridin-2-yl]-amine	+++
(5-Methoxy-[2,2']bipyridinyl-6-yl)-[5-(4-methyl-piperazin-1-yl)-pyridin-2-yl]-amine	+++
[2,3']Bipyridinyl-6'-yl-(3-methoxy-6-thiazol-2-yl-pyridin-2-yl)-amine	+++
3-[6-(6-Thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-propionic acid ethyl ester	+++
(3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-amine	+++
(3-Methoxy-6-pyrazin-2-yl-pyridin-2-yl)-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-amine	+++
(3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-pyridin-2-yl-amine	+++
(5-Methoxy-[2,2']bipyridinyl-6-yl)-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-amine	+++
(5-Isopropyl-pyridin-2-yl)-(3-methoxy-6-thiazol-2-yl-pyridin-2-yl)-amine	+++
(5-Isopropyl-pyridin-2-yl)-(5-methoxy-[2,2']bipyridinyl-6-yl)-amine	+++
(5-Pyrrolidin-1-ylmethyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	+++
[6-(5-Isopropyl-thiazol-2-yl)-pyridin-2-yl]-pyridin-2-yl-amine	+++
[6-(5-Chloro-thiazol-2-yl)-3-methoxy-pyridin-2-yl]-pyridin-2-yl-amine	+++
[6-(5-Ethyl-thiazol-2-yl)-pyridin-2-yl]-pyridin-2-yl-amine	+++
6'-(6-Pyrazol-1-yl-pyridin-2-ylamino)-3,4,5,6-tetrahydro-[1,3']bipyridinyl-2-one	+++

[6-(5-Chloro-thiazol-2-yl)-pyridin-2-yl]-(5-morpholin-4-yl-pyridin-2-yl)-amine	+++
N^2-[6-(5-Chloro-thiazol-2-yl)-pyridin-2-yl]-N^5-(2-methoxy-ethyl)-N^5-methyl-pyridine-2,5-diamine	+++
[6-(5-Chloro-thiazol-2-yl)-3-methoxy-pyridin-2-yl]-(4-methoxy-3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-amine	+++
[6-(5-Chloro-thiazol-2-yl)-3-methoxy-pyridin-2-yl]-(5-morpholin-4-yl-pyridin-2-yl)-amine	+++
[6-(5-Chloro-thiazol-2-yl)-3-methoxy-pyridin-2-yl]-(5-pyrrolidin-1-yl-pyridin-2-yl)-amine	+++
1-{6-[6-(5-Chloro-thiazol-2-yl)-3-methoxy-pyridin-2-ylamino]-pyridin-3-yl}-pyrrolidin-2-one	+++
(3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-amine	+++
(5-Chloro-pyridin-2-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine	++
(5-Phenyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	++
[6-(4-Methyl-pyrazol-1-yl)-pyridin-2-yl]-(4-methyl-3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-amine	++
6'-(6-Chloro-1H-benzoimidazol-2-yl)-5-methyl-[2,2']bipyridinyl	++
[5-(2-Methoxy-phenyl)-pyridin-2-yl]-(6-thiazol-2-yl-pyridin-2-yl)-amine	++
(5-Cyclopropyl-[1,3,4]thiadiazol-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	++
(5-tert-Butyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	++
6-(6-Pyrazol-1-yl-pyridin-2-ylamino)-nicotinic acid methyl ester	++
(5-Isopropyl-pyridin-2-yl)-(3-methoxy-6-pyrazin-2-yl-pyridin-2-yl)-amine	++
[6-(5-Chloro-thiazol-2-yl)-pyridin-2-yl]-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-amine	++
(3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-(5-phenyl-pyridin-2-yl)-amine	++
[6-(5-Methyl-thiazol-2-yl)-pyridin-2-yl]-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-amine	++
[6-(5-Chloro-thiazol-2-yl)-3-methoxy-pyridin-2-yl]-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-amine	++
4-Methyl-1-[6-(6-thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-piperazin-2-one	++
6'-[6-(5-Ethyl-thiazol-2-yl)-pyridin-2-ylamino]-3,4,5,6-tetrahydro-[1,3']bipyridinyl-2-one	++
(5-Isopropyl-pyridin-2-yl)-(3-methoxy-6-thiazol-2-yl-pyridin-2-yl)-amine	++

5-[(Benzylamino)methyl]-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine dihydrochloride	++
(5-Cyclopropyl-[1,3,4]thiadiazol-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	++
(3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-[5-(4-methyl-[1,4]diazepan-1-yl)-pyridin-2-yl]-amine	++
1-Methyl-4-[6-(6-thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-[1,4]diazepan-5-one	++
1-[6-(6-Thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-piperazin-2-one	++
N^5-(1-Aza-bicyclo[2.2.2]oct-3-yl)-N^2-(3-methoxy-6-thiazol-2-yl-pyridin-2-yl)-pyridine-2,5-diamine	++
N^2-(3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-N^5-methyl-N^5-(1-methyl-pyrrolidin-3-yl)-pyridine-2,5-diamine	++
(3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-[5-(3-methyl-piperazin-1-yl)-pyridin-2-yl]-amine	++
[5-(4-Methyl-piperazin-1-yl)-pyridin-2-yl]-(6-pyrazol-1-yl-pyridin-2-yl)-amine	+
(6-Fluoro-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	+

Key: + indicates 1.0 μM>IC50>0.5 μM; ++ indicates 0.5 μM>IC50>0.1 μM; +++ indicates 0.1 μM>IC50>0.03 μM; ++++ indicates 0.03 μM>IC50>0.0 μM.

EXAMPLE 25

25.1 Assay for Compound Activity in an Electroconvulsive Shock-Passive/Avoidance Model

[0331] The effects of compounds of the invention were studied on learning and memory formation for a passive avoidance task in mice following electroconvulsive shock training utilizing a modification of the protocol described by Inan, *et al.*, *Eur. J. Pharmacol.*,(2000), 407(1-2): 159-64.

25.2 Results

[0332] Compounds tested in this assay, along with their *in vivo* inhibitory activity, are provided in Table 2.

Table 2

Compound Name	*In Vivo* Inhibitory Activity (minimum effective dose, (MED))
(6-Thiazol-2-yl-pyridin-2-yl)-(5-thiophen-3-yl-pyridin-2-yl)-amine	++++
(3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-[5-(4-methyl-piperazin-1-yl)-pyridin-2-yl]-amine	++++
(5,6,7,8-Tetrahydro-isoquinolin-3-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	++++
(3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-amine	++++
(3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-(5-morpholin-4-yl-pyridin-2-yl)-amine	++++
(5-Pyrrolidin-1-ylmethyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	++++
1-{6-[6-(5-Chloro-thiazol-2-yl)-pyridin-2-ylamino]-pyridin-3-yl}-pyrrolidin-2-one	++++
4-Methyl-1-[6-(6-thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-piperazin-2-one	++++
[6-(5-Chloro-thiazol-2-yl)-3-methoxy-pyridin-2-yl]-(5-pyrrolidin-1-yl-pyridin-2-yl)-amine	++++
[5-(1,3-Dihydro-isoindol-2-ylmethyl)-pyridin-2-yl]-(6-thiazol-2-yl-pyridin-2-yl)-amine	++++
1-Methyl-4-[6-(6-thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-[1,4]diazepan-5-one	++++
(3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-(5-pyrrolidin-1-yl-pyridin-2-yl)-amine	++++
(5-Phenyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	+++
(5-Bromo-pyridin-2-yl)-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine	+++
(5-Chloro-pyridin-2-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine	+++
[5-(3-Fluoro-phenyl)-pyridin-2-yl]-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine	+++
1-[6-(6-Thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-piperazin-2-one	+++
1-[6-(3-Methoxy-6-thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-pyrrolidin-2-one	+++

[6-(5-Chloro-thiazol-2-yl)-pyridin-2-yl]-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-amine	+++
(5-Chloro-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	++
[5-(2-Methoxy-phenyl)-pyridin-2-yl]-(6-thiazol-2-yl-pyridin-2-yl)-amine	++
(5-Chloro-pyridin-2-yl)-(6-pyrazol-1-yl-pyridin-2-yl)-amine	+
(5-Methyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine	+

Key: + indicates 100.0 mg/kg ip >MED>20.0 mg/kg ip;

++ indicates 20.0 mg/kg ip >MED>2.0 mg/kg ip;

+++ indicates 2.0 mg/kg ip >MED>1.0 mg/kg ip;

++++ indicates 1.0 mg/kg ip >MED>0.05 mg/kg ip.

EXAMPLE 26

26.1 Compund List

[0333] Example 26 sets forth representative compounds of the invention.

Compound #	Compound Name
1	(6'-Bromo-[2,2']bipyridinyl-6-yl)-pyridin-2-yl-amine
2	[2,2']Bipyridinyl-6-yl-pyridin-2-yl-amine
3	N^6,$N^{6'}$-Di-pyridin-2-yl-[2,2']bipyridinyl-6,6'-diamine
4	N,N'-Di-pyridin-2-yl-pyridine-2,6-diamine
5	(6'-Bromo-[2,2']bipyridinyl-6-yl)-(5-fluoro-pyridin-2-yl)-amine
6	(6'-Bromo-[2,2']bipyridinyl-6-yl)-(5-chloro-pyridin-2-yl)-amine
7	(6'-Bromo-[2,2']bipyridinyl-6-yl)-(4-methyl-pyridin-2-yl)-amine
8	[2,2']Bipyridinyl-6-yl-(5-fluoro-pyridin-2-yl)-amine
9	[2,2']Bipyridinyl-6-yl-(4-methyl-pyridin-2-yl)-amine
10	[2,2']Bipyridinyl-6-yl-(5-chloro-pyridin-2-yl)-amine

11	{[2,2']Bipyridinyl-6-yl-pyridin-2-yl-amine}$_2$ Zn(II) Complex
12	{[2,2']Bipyridinyl-6-yl-pyridin-2-yl-amine}$_2$ Fe(II) Complex
13	2-Amino-[1,2';6',2"]terpyridin-1-ylium; bromide
14	(6'-Bromo-[2,2']bipyridinyl-6-yl)-methyl-pyridin-2-yl-amine
15	N,N'-Dimethyl-N,N'-di-pyridin-2-yl-pyridine-2,6-diamine
16	(6'-Bromo-[2,2']bipyridinyl-6-yl)-(5-phenyl-pyridin-2-yl)-amine
17	[2,2']Bipyridinyl-6-yl-methyl-pyridin-2-yl-amine
18	[2,2']Bipyridinyl-6-yl-(5-phenyl-pyridin-2-yl)-amine
19	[2,2']Bipyridinyl-6-yl-(5-iodo-pyridin-2-yl)-amine
20	(5'-Chloro-[2,2']bipyridinyl-6-yl)-(5-chloro-pyridin-2-yl)-amine
21	(5-Chloro-pyridin-2-yl)-(5'-trifluoromethyl-[2,2']bipyridinyl-6-yl)-amine
22	(5-Chloro-pyridin-2-yl)-(5'-morpholin-4-yl-[2,2']bipyridinyl-6-yl)-amine
23	[2,2']Bipyridinyl-6-yl-[5-(3-fluoro-phenyl)-pyridin-2-yl]-amine
24	[2,2']Bipyridinyl-6-yl-[5-(2-fluoro-phenyl)-pyridin-2-yl]-amine
25	[6-(5-Methyl-[1,2,4]oxadiazol-3-yl)-pyridin-2-yl]-(5-phenyl-pyridin-2-yl)-amine
26	(5-Chloro-pyridin-2-yl)-[6-(5-methyl-[1,2,4]oxadiazol-3-yl)-pyridin-2-yl]-amine
27	[2,2']Bipyridinyl-6-yl-[5-(4-fluoro-phenyl)-pyridin-2-yl]-amine
28	(5-Chloro-pyridin-2-yl)-(6-pyrimidin-2-yl-pyridin-2-yl)-amine
29	(5-Chloro-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine
30	(5-Chloro-pyridin-2-yl)-[6-(1-methyl-1H-imidazol-4-yl)-pyridin-2-yl]-amine
31	[2,2']Bipyridinyl-6-yl-pyrazin-2-yl-amine
32	[2,2']Bipyridinyl-6-yl-(5-iodo-4-methyl-pyridin-2-yl)-amine

33	[2,2']Bipyridinyl-6-yl-(5-iodo-3-methyl-pyridin-2-yl)-amine
34	(5-Chloro-pyridin-2-yl)-(6-pyrazol-1-yl-pyridin-2-yl)-amine
35	[2,2']Bipyridinyl-6-yl-(3,5-dichloro-pyridin-2-yl)-amine
36	(5-Phenyl-pyridin-2-yl)-(6-pyrazol-1-yl-pyridin-2-yl)-amine
37	[2,2']Bipyridinyl-6-yl-(5-iodo-pyridin-2-yl)-carbamic acid tert-butyl ester
38	[2,2']Bipyridinyl-6-yl-(5-iodo-4-methyl-pyridin-2-yl)-carbamic acid tert-butyl ester
39	[2,2']Bipyridinyl-6-yl-[5-(4-fluoro-phenyl)-4-methyl-pyridin-2-yl]-carbamic acid tert-butyl ester
40	(5-Chloro-pyridin-2-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine
41	(5-Phenyl-pyridin-2-yl)-(6-pyrimidin-2-yl-pyridin-2-yl)-amine
42	(5-Phenyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine
43	(5-Phenyl-pyridin-2-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine
44	N-[2,2']Bipyridinyl-6-yl-N-(5-iodo-pyridin-2-yl)-acetamide
45	[2,2']Bipyridinyl-6-yl-[5-(4-fluoro-phenyl)-4-methyl-pyridin-2-yl]-amine
46	4-Methyl-6-(4-methyl-pyridin-2-ylamino)-[2,2']bipyridinyl-5-carbonitrile
47	4-Methyl-6-(pyridin-2-ylamino)-[2,2']bipyridinyl-5-carbonitrile
48	6-(5-Chloro-pyridin-2-ylamino)-4-methyl-[2,2']bipyridinyl-5-carbonitrile
49	6-(5-Fluoro-pyridin-2-ylamino)-4-methyl-[2,2']bipyridinyl-5-carbonitrile
50	6-(3,5-Dichloro-pyridin-2-ylamino)-4-methyl-[2,2']bipyridinyl-5-carbonitrile
51	(5-Fluoro-pyridin-2-yl)-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine
52	[2,2']Bipyridinyl-6-yl-[5-(4-dimethylamino-phenyl)-4-methyl-pyridin-2-yl]-amine

53 (5-Chloro-pyridin-2-yl)-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine

54 [5-(4-Fluoro-phenyl)-4-methyl-pyridin-2-yl]-(6-pyrazol-1-yl-pyridin-2-yl)-amine

55 [4-Methyl-5-(4'-dimethyl amino)phenyl-pyridin-2-yl]-(6-pyrazol-1-yl-pyridin-2-yl)-amine

56 2,6-Bis-thiazol-2-yl-pyridine

57 (5-Bromo-3,4-dimethyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine

58 (5-Bromo-pyrimidin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine

59 (5-Fluoro-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine

60 (5-Bromo-pyridin-2-yl)-(6-pyrazol-1-yl-pyridin-2-yl)-amine

61 (5-Bromo-pyridin-2-yl)-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine

62 (4-Methyl-3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine

63 (5-Fluoro-pyridin-2-yl)-(6-pyrazol-1-yl-pyridin-2-yl)-amine

64 (5-Morpholin-4-yl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine

65 (6-Thiazol-2-yl-pyridin-2-yl)-(5-thiophen-2-yl-pyridin-2-yl)-amine

66 [3,3']Bipyridinyl-6-yl-(6-thiazol-2-yl-pyridin-2-yl)-amine

67 (5-Isopropenyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine

68 (5-Isopropyl-pyridin-2-yl)-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine

69 (5-Fluoro-pyridin-2-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine

70 (5-Bromo-pyridin-2-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine

71 [3,3']Bipyridinyl-6-yl-(6-pyrazin-2-yl-pyridin-2-yl)-amine

72 (5-Isopropenyl-pyridin-2-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine

73 (6-Pyrazin-2-yl-pyridin-2-yl)-(5-thiophen-2-yl-pyridin-2-yl)-amine

74 (5-Morpholin-4-yl-pyridin-2-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine

75 (5-Isopropyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine

76 [6-(4-Methyl-pyrazol-1-yl)-pyridin-2-yl]-(5-phenyl-pyridin-2-yl)-amine

77 (5-Isopropenyl-pyridin-2-yl)-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine

78 (5-Methoxy-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine

79 [5-(4-Methyl-piperazin-1-yl)-pyridin-2-yl]-(6-thiazol-2-yl-pyridin-2-yl)-amine

80 (5-Methoxy-pyridin-2-yl)-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine

81 (5-Isopropyl-pyridin-2-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine

82 [6-(4-Methyl-pyrazol-1-yl)-pyridin-2-yl]-(4-methyl-3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-amine

83 [5-(4-Methyl-piperazin-1-yl)-pyridin-2-yl]-(6-pyrazin-2-yl-pyridin-2-yl)-amine

84 [5-(4-Methyl-piperazin-1-yl)-pyridin-2-yl]-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine

85 [5-(4-Methyl-piperazin-1-yl)-pyridin-2-yl]-(6-pyrazol-1-yl-pyridin-2-yl)-amine

86 [6-(4-Methyl-pyrazol-1-yl)-pyridin-2-yl]-(5-morpholin-4-yl-pyridin-2-yl)-amine

87 [5-(3-Fluoro-phenyl)-pyridin-2-yl]-(6-thiazol-2-yl-pyridin-2-yl)-amine

88 [5-(2-Methoxy-phenyl)-pyridin-2-yl]-(6-thiazol-2-yl-pyridin-2-yl)-amine

89 (5-Pyrrolidin-1-yl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine

90 [6-(4-Methyl-pyrazol-1-yl)-pyridin-2-yl]-(5-pyrrolidin-1-yl-pyridin-2-yl)-amine

91 (6-Thiazol-2-yl-pyridin-2-yl)-(5-thiophen-3-yl-pyridin-2-yl)-amine

92 (5-Furan-2-yl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine

93 [5-(5-Methyl-furan-2-yl)-pyridin-2-yl]-(6-thiazol-2-yl-pyridin-2-yl)-amine

94	1-[6-(6-Thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-pyrrolidin-2-one
95	(6-Fluoro-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine
96	[5-(3-Fluoro-phenyl)-pyridin-2-yl]-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine
97	[5-(2-Methoxy-phenyl)-pyridin-2-yl]-[6-(4-methyl-pyrazol-1-yl)-pyridin-2-yl]-amine
98	(5-Phenyl-2H-pyrazol-3-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine
99	(6-Thiazol-2-yl-pyridin-2-yl)-[2-(6-thiazol-2-yl-pyridin-2-yl)-2H-pyrazol-3-yl]-amine
100	(5-Bromo-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine
101	6-([2,2']Bipyridinyl-6-ylamino)-N,N-diethyl-nicotinamide
102	N,N-Diethyl-6-(6-pyrazin-2-yl-pyridin-2-ylamino)-nicotinamide
103	(4-Methyl-thiazol-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine
104	1-[6-(6-Pyrazin-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-pyrrolidin-2-one
105	N,N-Diethyl-6-(6-thiazol-2-yl-pyridin-2-ylamino)-nicotinamide
106	(6-Pyrazin-2-yl-pyridin-2-yl)-(5-pyrrolidin-1-yl-pyridin-2-yl)-amine
107	(6-Pyrazin-2-yl-pyridin-2-yl)-(5-thiophen-3-yl-pyridin-2-yl)-amine
108	(5-Furan-2-yl-pyridin-2-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine
109	[5-(3-Fluoro-phenyl)-pyridin-2-yl]-(6-pyrazin-2-yl-pyridin-2-yl)-amine
110	[5-(2-Methoxy-phenyl)-pyridin-2-yl]-(6-pyrazin-2-yl-pyridin-2-yl)-amine
111	[5-(5-Methyl-furan-2-yl)-pyridin-2-yl]-(6-pyrazin-2-yl-pyridin-2-yl)-amine
112	(4-Methyl-3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine
113	(5-Ethoxy-6-fluoro-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine
114	Isoquinolin-3-yl-(6-thiazol-2-yl-pyridin-2-yl)-amine

115 (4-Phenyl-thiazol-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine

116 (5-tert-Butyl-isoxazol-3-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine

117 (5-Cyclopropyl-[1,3,4]thiadiazol-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine

118 (5,6,7,8-Tetrahydro-isoquinolin-3-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine

119 [1,10]Phenanthrolin-2-yl-pyridin-2-yl-amine

120 (6-Thiazol-2-yl-pyridin-2-yl)-(5-trifluoromethyl-[1,3,4]thiadiazol-2-yl)-amine

121 (6-Thiazol-2-yl-pyridin-2-yl)-[1,2,4]triazol-4-yl-amine

122 (5-tert-Butyl-isoxazol-3-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine

123 3,5-Di-pyridin-2-yl-3H-imidazo[4,5-b]pyridine

124 (5-Nitro-[2,2']bipyridinyl-6-yl)-pyridin-2-yl-amine

125 3,5-Di-pyridin-2-yl-3H-imidazo[4,5-b]pyridine

126 N^6-Pyridin-2-yl-[2,2']bipyridinyl-5,6-diamine

127 N-[6-(Pyridin-2-ylamino)-[2,2']bipyridinyl-5-yl]-acetamide

128 (5-Methoxy-[2,2']bipyridinyl-6-yl)-pyridin-2-yl-amine

129 6-(Pyridin-2-ylamino)-[2,2']bipyridinyl-5-carboxylic acid methyl ester

130 6-(Pyridin-2-ylamino)-[2,2']bipyridinyl-5-carboxylic acid dimethylamide

131 (5-Isopropoxy-[2,2']bipyridinyl-6-yl)-pyridin-2-yl-amine

132 (5-Benzyloxy-[2,2']bipyridinyl-6-yl)-pyridin-2-yl-amine

133 [5-(2-Methoxy-ethoxy)-[2,2']bipyridinyl-6-yl]-pyridin-2-yl-amine

134 [2,2']Bipyridinyl-6-yl-di-pyridin-2-yl-amine

135 6-(Pyridin-2-ylamino)-[2,2']bipyridinyl-5-ol

136 [6-(Pyridin-2-ylamino)-[2,2']bipyridinyl-5-yloxy]-acetic acid methyl ester

137	4,6-Di-pyridin-2-yl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazine
138	(5-Bromo-pyridin-2-yl)-(5-methoxy-[2,2']bipyridinyl-6-yl)-amine
139	(5-Methoxy-[2,2']bipyridinyl-6-yl)-(5-phenyl-pyridin-2-yl)-amine
140	[5-(3-Fluoro-phenyl)-pyridin-2-yl]-(5-methoxy-[2,2']bipyridinyl-6-yl)-amine
141	[2,2']Bipyridinyl-6-yl-(5-nitro-pyridin-2-yl)-amine
142	(5-Methyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine
143	6-(6-Thiazol-2-yl-pyridin-2-ylamino)-nicotinic acid methyl ester
144	[6-(6-Thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-methanol
145	(5-Hexyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine
146	(5-tert-Butyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine
147	(5-Ethyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine
148	(5-Methyl-pyridin-2-yl)-(6-pyrazol-1-yl-pyridin-2-yl)-amine
149	6-(6-Pyrazol-1-yl-pyridin-2-ylamino)-nicotinic acid methyl ester
150	[5-(2-Benzyloxy-ethyl)-pyridin-2-yl]-(6-thiazol-2-yl-pyridin-2-yl)-amine
151	(5-Methyl-pyridin-2-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine
152	2-[6-(6-Thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-ethanol
153	3-[6-(6-Thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-propionic acid ethyl ester
154	3-[6-(6-Thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-propan-1-ol
155	[5-(2-Pyrrolidin-1-yl-ethyl)-pyridin-2-yl]-(6-thiazol-2-yl-pyridin-2-yl)-amine
156	(3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-pyridin-2-yl-amine
157	(3-Methoxy-6-pyrazin-2-yl-pyridin-2-yl)-pyridin-2-yl-amine
158	(1'-Methyl-1',2',3',4',5',6'-hexahydro-[3,3']bipyridinyl-6-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine

159 (1'-Methyl-1',2',3',4',5',6'-hexahydro-[3,3']bipyridinyl-6-yl)-(6-pyrazin-2-yl-pyridin-2-yl)-amine

160 [2,3']Bipyridinyl-6'-yl-(6-thiazol-2-yl-pyridin-2-yl)-amine

161 [2,3']Bipyridinyl-6'-yl-(6-pyrazin-2-yl-pyridin-2-yl)-amine

162 (3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-amine

163 (3-Methoxy-6-pyrazin-2-yl-pyridin-2-yl)-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-amine

164 (5-Methoxy-[2,2']bipyridinyl-6-yl)-(3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl-6'-yl)-amine

165 (5-Isopropyl-pyridin-2-yl)-(3-methoxy-6-thiazol-2-yl-pyridin-2-yl)-amine

166 (5-Isopropyl-pyridin-2-yl)-(3-methoxy-6-pyrazin-2-yl-pyridin-2-yl)-amine

167 (5-Isopropyl-pyridin-2-yl)-(5-methoxy-[2,2']bipyridinyl-6-yl)-amine

168 (3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-(5-morpholin-4-yl-pyridin-2-yl)-amine

169 (3-Methoxy-6-pyrazin-2-yl-pyridin-2-yl)-(5-morpholin-4-yl-pyridin-2-yl)-amine

170 (5-Methoxy-[2,2']bipyridinyl-6-yl)-(5-morpholin-4-yl-pyridin-2-yl)-amine

171 (5-Pyrrolidin-1-ylmethyl-pyridin-2-yl)-(6-thiazol-2-yl-pyridin-2-yl)-amine

172 (3-Methoxy-6-thiazol-2-yl-pyridin-2-yl)-[5-(4-methyl-piperazin-1-yl)-pyridin-2-yl]-amine

173 (3-Methoxy-6-pyrazin-2-yl-pyridin-2-yl)-[5-(4-methyl-piperazin-1-yl)-pyridin-2-yl]-amine

174 (5-Methoxy-[2,2']bipyridinyl-6-yl)-[5-(4-methyl-piperazin-1-yl)-pyridin-2-yl]-amine

175 N^5-(2-Methoxy-ethyl)-N^2-(3-methoxy-6-thiazol-2-yl-pyridin-2-yl)-N^5-methyl-pyridine-2,5-diamine

176 [2,3']Bipyridinyl-6'-yl-(3-methoxy-6-thiazol-2-yl-pyridin-2-yl)-amine

177 6-(5-Chloro-1,3-thiazol-2-yl)-N-pyridin-2-ylpyridin-2-amine hydrochloride

178 3-Methoxy-N-(5-pyrrolidin-1-ylpyridin-2-yl)-6-(1,3-thiazol-2-yl)pyridin-2-amine trihydrochloride

179 1-(6-{[3-Methoxy-6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)pyrrolidin-2-one dihydrochloride

180 6-(5-Isopropyl-1,3-thiazol-2-yl)-N-pyridin-2-ylpyridin-2-amine dihydrochloride

181 1-(6-{[3-Methoxy-6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)piperidin-2-one dihydrochloride

182 1-(6-{[3-Methoxy-6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)piperidin-4-ol trihydrochloride

183 6-(5-Methyl-1,3-thiazol-2-yl)-N-pyridin-2-ylpyridin-2-amine dihydrochloride

184 6-(5-Chloro-1,3-thiazol-2-yl)-3-methoxy-N-pyridin-2-ylpyridin-2-amine dihydrochloride

185 6-(5-Ethyl-1,3-thiazol-2-yl)-N-pyridin-2-ylpyridin-2-amine dihydrochloride

186 1-(6-{[6-(1H-Pyrazol-1-yl)pyridin-2-yl]amino}pyridin-3-yl)piperidin-2-one monohydrochloride

187 5-Methoxy-N-(5-morpholin-4-ylpyridin-2-yl)-6-(1H-pyrazol-1-yl)pyridin-2-amine dihydrochloride

188 3-Methoxy-N-[5-(4-methoxypiperidin-1-yl)pyridin-2-yl]-6-(1,3-thiazol-2-yl)pyridin-2-amine trihydrochloride

189 N-[6-(5-Isopropyl-1,3-thiazol-2-yl)pyridin-2-yl]-5-morpholin-4-ylpyridin-2-amine dihydrochloride

190 N-[6-(5-Isopropyl-1,3-thiazol-2-yl)pyridin-2-yl]-5-piperidin-1-ylpyridin-2-amine dihydrochloride

191 N-[6-(5-Isopropyl-1,3-thiazol-2-yl)pyridin-2-yl]-5-pyrrolidin-1-ylpyridin-2-amine dihydrochloride

192 1-(6-{[6-(5-Isopropyl-1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)pyrrolidin-2-one dihydrochloride

193 1-(6-{[6-(5-Isopropyl-1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)piperidin-2-one dihydrochloride

194 N-[6-(5-Chloro-1,3-thiazol-2-yl)pyridin-2-yl]-5-morpholin-4-ylpyridin-2-amine dihydrochloride

195 N-[6-(5-Chloro-1,3-thiazol-2-yl)pyridin-2-yl]-5-piperidin-1-ylpyridin-2-amine dihydrochloride

196 N-[6-(5-Chloro-1,3-thiazol-2-yl)pyridin-2-yl]-5-pyrrolidin-1-ylpyridin-2-amine dihydrochloride

197 1-(6-{[6-(5-Chloro-1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)pyrrolidin-2-one dihydrochloride

198 1-(6-{[6-(5-Chloro-1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)piperidin-2-one dihydrochloride

199 1-(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)piperidin-2-one trihydrochloride

200 N^5-(2-Methoxyethyl)-N^5-methyl-N^2-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridine-2,5-diamine trihydrochloride

201 1-(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)piperidin-4-ol trihydrochloride

202 5-(4-Methoxypiperidin-1-yl)-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine trihydrochloride

203 3-Methoxy-N-(5-phenylpyridin-2-yl)-6-(1,3-thiazol-2-yl)pyridin-2-amine dihydrochloride

204 N-[6-(5-Chloro-1,3-thiazol-2-yl)pyridin-2-yl]-5-(4-methylpiperazin-1-yl)pyridin-2-amine dihydrochloride

205 N-[6-(5-Isopropyl-1,3-thiazol-2-yl)pyridin-2-yl]-5-(4-methylpiperazin-1-yl)pyridin-2-amine dihydrochloride

206 N-[6-(5-Methyl-1,3-thiazol-2-yl)pyridin-2-yl]-5-piperidin-1-ylpyridin-2-amine trihydrochloride

207 5-(4-Methylpiperazin-1-yl)-N-[6-(5-methyl-1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine trihydrochloride

208 N-[6-(5-Methyl-1,3-thiazol-2-yl)pyridin-2-yl]-5-pyrrolidin-1-ylpyridin-2-amine dihydrochloride

209 1-(6-{[6-(5-Methyl-1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)pyrrolidin-2-one dihydrochloride

210 1-(6-{[6-(5-Methyl-1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)piperidin-2-one trihydrochloride

211 N^2-[6-(5-Chloro-1,3-thiazol-2-yl)pyridin-2-yl]-N^5-(2-methoxyethyl)-N^5-methylpyridine-2,5-diamine dihydrochloride

212 N^5-(2-Methoxyethyl)-N^5-methyl-N^2-[6-(5-methyl-1,3-thiazol-2-yl)pyridin-2-yl]pyridine-2,5-diamine trihydrochloride

213 N^2-[6-(5-Isopropyl-1,3-thiazol-2-yl)pyridin-2-yl]-N^5-(2-methoxyethyl)-N^5-methylpyridine-2,5-diamine trihydrochloride

214 N^2-[6-(5-Chloro-1,3-thiazol-2-yl)-3-methoxypyridin-2-yl]-N^5-(2-methoxyethyl)-N^5-methylpyridine-2,5-diamine trihydrochloride

215 6-(5-Chloro-1,3-thiazol-2-yl)-3-methoxy-N-(5-piperidin-1-ylpyridin-2-yl)pyridin-2-amine dihydrochloride

216 5-(4-Isopropylpiperazin-1-yl)-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine trihydrochloride

217 N-[5-(4-Isopropylpiperazin-1-yl)pyridin-2-yl]-3-methoxy-6-(1,3-thiazol-2-yl)pyridin-2-amine trihydrochloride

218 4-Methyl-1-(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)piperazin-2-one dihydrochloride

219 1-(6-{[3-Methoxy-6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)-4-methylpiperazin-2-one tetrahydrochloride

220 6-(5-Chloro-1,3-thiazol-2-yl)-3-methoxy-N-(5-morpholin-4-ylpyridin-2-yl)pyridin-2-amine dihydrochloride

221 6-(5-Chloro-1,3-thiazol-2-yl)-3-methoxy-N-(5-piperidin-1-ylpyridin-2-yl)pyridin-2-amine dihydrochloride

222 6-(5-Chloro-1,3-thiazol-2-yl)-3-methoxy-N-[5-(4-methylpiperazin-1-yl)pyridin-2-yl]pyridin-2-amine dihydrochloride

223 6-(5-Chloro-1,3-thiazol-2-yl)-3-methoxy-N-(5-pyrrolidin-1-ylpyridin-2-yl)pyridin-2-amine dihydrochloride

224 1-(6-{[6-(5-Chloro-1,3-thiazol-2-yl)-3-methoxypyridin-2-yl]amino}pyridin-3-yl)pyrrolidin-2-one monohydrochloride

225 1-(6-{[6-(5-Chloro-1,3-thiazol-2-yl)-3-methoxypyridin-2-yl]amino}pyridin-3-yl)piperidin-2-one dihydrochloride

226 N-[6-(5-Methyl-1,3-thiazol-2-yl)pyridin-2-yl]-5-morpholin-4-ylpyridin-2-amine dihydrochloride

227 N-[6-(5-Ethyl-1,3-thiazol-2-yl)pyridin-2-yl]-5-piperidin-1-ylpyridin-2-amine dihydrochloride

228 N-[6-(5-Ethyl-1,3-thiazol-2-yl)pyridin-2-yl]-5-pyrrolidin-1-ylpyridin-2-amine dihydrochloride

229 1-(6-{[6-(5-Ethyl-1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)pyrrolidin-2-one dihydrochloride

230 1-(6-{[6-(5-Ethyl-1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)piperidin-2-one monohydrochloride

231 N-[6-(5-Ethyl-1,3-thiazol-2-yl)pyridin-2-yl]-5-morpholin-4-ylpyridin-2-amine monohydrochloride

232 N-[6-(5-Ethyl-1,3-thiazol-2-yl)pyridin-2-yl]-5-(4-methylpiperazin-1-yl)pyridin-2-amine trihydrochloride

233 5-[(Benzylamino)methyl]-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine dihydrochloride

234 5-[(Cyclohexylamino)methyl]-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine dihydrochloride

235 5-[(Ethylamino)methyl]-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine dihydrochloride

236 5-(4-Methyl-1,4-diazepan-1-yl)-N-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine trihydrochloride

237 3-Methoxy-N-[5-(4-methyl-1,4-diazepan-1-yl)pyridin-2-yl]-6-(1,3-thiazol-2-yl)pyridin-2-amine tetrahydrochloride

238 1-(6-{[6-(5-Chloro-1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)-4-methylpiperazin-2-one dihydrochloride

239 1-(6-{[6-(5-Chloro-1,3-thiazol-2-yl)-3-methoxypyridin-2-yl]amino}pyridin-3-yl)-4-methylpiperazin-2-one hydrochloride

240 4-Methyl-1-(6-{[6-(4-methyl-1H-pyrazol-1-yl)pyridin-2-yl]amino}pyridin-3-yl)piperazin-2-one dihydrochloride

241 4-Methyl-1-(6-{[6-(1H-pyrazol-1-yl)pyridin-2-yl]amino}pyridin-3-yl)piperazin-2-one dihydrochloride

242 1-Methyl-4-(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)-1,4-diazepan-5-one dihydrochloride

243 4-(6-{[3-Methoxy-6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)-1-methyl-1,4-diazepan-5-one dihydrochloride

244 1-(6-{[6-(4-Bromo-1H-pyrazol-1-yl)pyridin-2-yl]amino}pyridin-3-yl)-4-methylpiperazin-2-one dihydrochloride

245 1-(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)piperazin-2-one dihydrochloride

246 1-(6-{[3-Methoxy-6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)piperazin-2-one dihydrochloride

247 3-Methoxy-N-(5-piperazin-1-ylpyridin-2-yl)-6-(1,3-thiazol-2-yl)pyridin-2-amine dihydrochloride

248 N-{5-[3-(Dimethylamino)pyrrolidin-1-yl]pyridin-2-yl}-3-methoxy-6-(1,3-thiazol-2-yl)pyridin-2-amine dihydrochloride

249 N^5-1-Azabicyclo[2.2.2]oct-3-yl-N^2-[3-methoxy-6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridine-2,5-diamine trihydrochloride

250 3-Methoxy-6-(1,3-thiazol-2-yl)-N-[5-(2,4,5-trimethylpiperazin-1-yl)pyridin-2-yl]pyridin-2-amine trihydrochloride

251 N^2-[3-Methoxy-6-(1,3-thiazol-2-yl)pyridin-2-yl]-N^5-methyl-N^5-(1-methylpyrrolidin-3-yl)pyridine-2,5-diamine trihydrochloride

252 3-Methoxy-*N*-[5-(3-methylpiperazin-1-yl)pyridin-2-yl]-6-(1,3-thiazol-2-yl)pyridin-2-amine dihydrochloride

253 *N*-[5-(3,5-Dimethylpiperazin-1-yl)pyridin-2-yl]-3-methoxy-6-(1,3-thiazol-2-yl)pyridin-2-amine dihydrochloride

254 4-[6-(3-Methoxy-6-thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-1-methyl-piperazin-2-one

255 4-[6-(6-Thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-[1,4]diazepan-5-one

256 4-[6-(3-Methoxy-6-thiazol-2-yl-pyridin-2-ylamino)-pyridin-3-yl]-[1,4]diazepan-5-one

257 1-{6-[6-(5-Bromo-thiazol-2-yl)-pyridin-2-ylamino]-pyridin-3-yl}-4-methyl-piperazin-2-one

258 1-{6-[6-(5-Bromo-thiazol-2-yl)-3-methoxy-pyridin-2-ylamino]-pyridin-3-yl}-4-methyl-piperazin-2-one

259 1-{6-[6-(5-Fluoro-thiazol-2-yl)-3-methoxy-pyridin-2-ylamino]-pyridin-3-yl}-4-methyl-piperazin-2-one

260 5-[(Benzylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

261 5-{[(2-Fluorobenzyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

262 5-{[(2-Methoxybenzyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

263 5-{[(3-Fluorobenzyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

264 5-{[(3-Methoxybenzyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

265 5-{[(4-Fluorobenzyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

266 5-{[(4-Methoxybenzyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

267 5-{[(1,3-Benzodioxol-5-ylmethyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

268 5-{[(2-Furylmethyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

269 *N*-[6-(1,3-Thiazol-2-yl)pyridin-2-yl]-5-{[(2-thienylmethyl)amino]methyl}pyridin-2-amine

270 5-{[(Pyridin-3-ylmethyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

271 5-{[(2-Phenylethyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

272 5-({[2-(2-Fluorophenyl)ethyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

273 5-({[2-(2-Methoxyphenyl)ethyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

274 5-({[2-(3-Fluorophenyl)ethyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

275 5-({[2-(3-Methoxyphenyl)ethyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

276 5-({[2-(4-Fluorophenyl)ethyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

277 5-({[2-(4-Methoxyphenyl)ethyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

278 *N*-[6-(1,3-Thiazol-2-yl)pyridin-2-yl]-5-({[2-(2-thienyl)ethyl]amino}methyl)pyridin-2-amine

279 5-({[2-(1*H*-Indol-3-yl)ethyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

280 5-{[(2-Pyridin-2-ylethyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

281 5-{[(2-Pyridin-3-ylethyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

282 5-{[(2-Pyridin-4-ylethyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

283 5-{[(3-Phenylpropyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

284 5-({[3-(1*H*-Imidazol-1-yl)propyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

285 5-{[(4-Phenylbutyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

286 5-({[2-(1*H*-Benzimidazol-2-yl)ethyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

287 5-[(Propylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

288 5-[(Isopropylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

289 5-[(*tert*-Butylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

290 5-{[(3-Methylbutyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

291 5-[(Pentylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

292 5-{[(1-Methylhexyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

293 5-{[(1-Propylbutyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

294 5-[(Cyclopentylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

295 *N*,*N*-Dimethyl-*N'*-[(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]cyclopentane-1,2-diamine

296 5-({[2-Pyrrolidin-1-ylcyclopentyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

297 5-({[2-Piperidin-1-ylcyclopentyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

298 5-({[2-(4-Methylpiperazin-1-yl)cyclopentyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

299 5-({[2-Morpholin-4-ylcyclopentyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

300 3-{[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]amino}dihydrofuran-2(3*H*)-one

301 5-({[(3*R*)-1-Benzylpyrrolidin-3-yl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

302 5-[(Cyclohexylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

303 5-({[2-Pyrrolidin-1-ylcyclohexyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

304 5-({[2-Piperidin-1-ylcyclohexyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

305 5-({[2-(4-Methylpiperazin-1-yl)cyclohexyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

306 5-({[2-Morpholin-4-ylcyclohexyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

307 *trans*-4-{[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]amino}cyclohexanol

308 5-{[(4-*tert*-Butylcyclohexyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

309 *N*,*N*-Dimethyl-*N*'-[(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]cyclohex-4-ene-1,2-diamine

310 5-{[(1-Benzylpiperidin-4-yl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

311 Ethyl 4-{[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]amino}piperidine-1-carboxylate

312 5-[(Cycloheptylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

313 5-[(Cyclooctylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

314 5-({[(1*S*)-1-Cyclohexylethyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

315 5-{[(1-Methyl-2-pyrrolidin-1-ylethyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

316 5-({[2-(3,4-Dihydroisoquinolin-2(1*H*)-yl)-1-methylethyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

317 5-({[1-Methyl-2-(4-methylpiperazin-1-yl)ethyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

318 5-({[1-Methyl-2-(4-phenylpiperazin-1-yl)ethyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

319 5-{[(1-Methyl-2-morpholin-4-ylethyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

320 2-{[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]amino}propan-1-ol

321 N^1,N^1-Diethyl-N^4-[(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]pentane-1,4-diamine

322 5-({[(1-Ethylpyrrolidin-2-yl)methyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

323 5-{[(2-Pyrrolidin-1-ylethyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

324 5-({[2-(1,3-Dihydro-2*H*-isoindol-2-yl)ethyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

325 5-({[2-(1-Methylpyrrolidin-2-yl)ethyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

326 5-{[(2-Piperidin-1-ylethyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

327 *N*-Ethyl-*N*-(3-methylphenyl)-*N'*-[(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]ethane-1,2-diamine

328 5-{[(2-Methoxyethyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

329 *N*,*N*-Diethyl-*N'*-[(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]propane-1,3-diamine

330 5-{[(3-Pyrrolidin-1-ylpropyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

331 1-(3-{[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]amino}propyl)pyrrolidin-2-one

332 5-({[3-(4-Methylpiperazin-1-yl)propyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

333 5-{[(3-Morpholin-4-ylpropyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

334 *N*,*N*-Dimethyl-*N'*-[(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]ethane-1,2-diamine

335 5-{[Benzyl(methyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

336 {Methyl[(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]amino}acetonitrile

337 Ethyl {Methyl[(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]amino}acetate

338 5-{[Methyl(2-phenylethyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

339 *N*,*N*-Diethyl-*N'*-methyl-*N'*-[(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]ethane-1,2-diamine

340 2-{Methyl[(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]amino}ethanol

341 5-{[(1-Benzylazetidin-3-yl)(methyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

342 5-{[Cyclohexyl(methyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

343 5-({Methyl[(1*R*,2*R*)-2-pyrrolidin-1-ylcyclohexyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

344 5-({Methyl[(1*R*,2*R*)-2-morpholin-4-ylcyclohexyl]amino}methyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

345 *N*,*N*,*N'*-Trimethyl-*N'*-[(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]cyclohex-4-ene-1,2-diamine

346 5-{[Methyl(1-methylpiperidin-4-yl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

347 5-[(Diethylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

348 5-{[Benzyl(ethyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

349 *N*,*N*,*N'*-Triethyl-*N'*-[(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]ethane-1,2-diamine

350 2-{Ethyl[(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]amino}ethanol

351 5-{[Cyclohexyl(ethyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

352 5-{[Benzyl(isopropyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

353 5-{[Isopropyl(2-methoxyethyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

354 5-{[Bis(2-methoxyethyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

355 5-[(Dibutylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

356 5-[(Dicyclohexylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

357 Diethyl 2,2'-{[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]imino}diacetate

358 3-{Benzyl[(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]amino}propanenitrile

359 2-{Benzyl[(6-{[6-(1,3-thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]amino}ethanol

360 5-[(Diisobutylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

361 5-[(Dipropylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

362 5-{[Ethyl(propyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

363 1-[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]azetidin-3-ol

364 5-[(3-Piperidin-1-ylazetidin-1-yl)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

365 5-(Pyrrolidin-1-ylmethyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

366 5-{[(2*S*)-2-(Methoxymethyl)pyrrolidin-1-yl]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

367 5-(1,3-Dihydro-2*H*-isoindol-2-ylmethyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

368 5-(Piperidin-1-ylmethyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

369 1-[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]piperidin-3-ol

370 5-[(4-Methylpiperidin-1-yl)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

371 1-[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]piperidine-4-carboxamide

372 Ethyl 1-[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]piperidine-4-carboxylate

373 1-[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]piperidin-4-ol

374 5-[(4-Benzylpiperidin-1-yl)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

375 5-(1,4'-Bipiperidin-1'-ylmethyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

376 5-[(2,6-Dimethylpiperidin-1-yl)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

377 5-[(2,2,6,6-Tetramethylpiperidin-1-yl)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

378 5-(3,6-Dihydropyridin-1(2*H*)-ylmethyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

379 5-[(4-Phenyl-3,6-dihydropyridin-1(2*H*)-yl)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

380 5-(3,4-Dihydroisoquinolin-2(1*H*)-ylmethyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

381 5-[(4-Methylpiperazin-1-yl)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

382 5-[(4-Isopropylpiperazin-1-yl)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

383 Ethyl 4-[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]piperazine-1-carboxylate

384 5-{[4-(2-Methoxyethyl)piperazin-1-yl]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

385 5-[(4-Phenylpiperazin-1-yl)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

386 5-{[4-(2-Methoxyphenyl)piperazin-1-yl]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

387 5-{[4-(3-Methoxyphenyl)piperazin-1-yl]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

388 5-[(4-Benzylpiperazin-1-yl)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

389 5-(Morpholin-4-ylmethyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

390 5-[(2,6-Dimethylmorpholin-4-yl)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

391 *N*-[6-(1,3-Thiazol-2-yl)pyridin-2-yl]-5-(thiomorpholin-4-ylmethyl)pyridin-2-amine

392 5-(Azepan-1-ylmethyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

393 5-[(4-Methyl-1,4-diazepan-1-yl)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

394 5-[(4-Propylpiperazin-1-yl)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

395 5-{[4-(2-Fluorobenzoyl)piperazin-1-yl]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

396 5-{[4-(3-Fluorobenzoyl)piperazin-1-yl]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

397 5-{[4-(4-Fluorobenzoyl)piperazin-1-yl]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

398 5-{[4-(3-Methoxypropyl)piperazin-1-yl]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

399 5-{[4-(2-Methoxybenzyl)piperazin-1-yl]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

400 5-{[4-(3-Methoxybenzyl)piperazin-1-yl]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

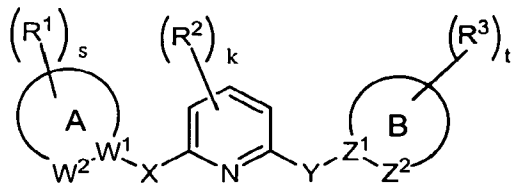
401 5-{[4-(4-Methoxybenzyl)piperazin-1-yl]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine

402	5-{[4-(Pyridin-4-ylmethyl)piperazin-1-yl]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine
403	{1-[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]piperidin-4-yl}methanol
404	5-(Anilinomethyl)-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine
405	5-{[(2-Methoxyphenyl)amino]methyl}-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine
406	5-[(1,3-Thiazol-2-ylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine
407	5-[(Pyridin-2-ylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine
408	5-[(Pyridin-3-ylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine
409	2-{4-[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]piperazin-1-yl}ethanol
410	5-[(Pyridin-4-ylamino)methyl]-*N*-[6-(1,3-thiazol-2-yl)pyridin-2-yl]pyridin-2-amine
411	*N*-[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]pyrazin-2-amine
412	*N*-[(6-{[6-(1,3-Thiazol-2-yl)pyridin-2-yl]amino}pyridin-3-yl)methyl]pyrimidin-2-amine

[0334] It is understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application and scope of the appended claims. All publications, patents, and patent applications cited herein are hereby incorporated by reference in their entirety for all purposes.

WHAT IS CLAIMED IS:

1. A compound according to Formula I:

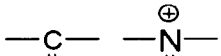
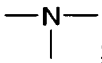


(I)

wherein

A and B are independently selected from substituted or unsubstituted 5- or 6-membered heterocyclic and heteroaryl rings,

wherein

W^1 and Z^1 are independently selected from  and  ;

W^2 and Z^2 are independently selected from -NH- and -N=;

X is selected from a bond and $-NR^4-$;

Y is selected from a bond and $-NR^5-$;

s and t are integers independently selected from 1-5;

k is an integer selected from 0-3;

R^2 is independently selected from OR^6, NR^7R^8, NO_2, $-SO_2NR^7R^8$, cyano, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted 3- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;

R^1, R^3, R^4 and R^5 are independently selected from H, OR^6, NR^7R^8, NO_2, $-SO_2NR^7R^8$, cyano, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted 3- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;

wherein R^6, R^7, and R^8 are independently selected from H, $-NO_2$, cyano, halogen, substituted or unsubstituted alkyl, substituted or

unsubstituted heteroalkyl, substituted or unsubstituted 3- to 7-membered cycloalkyl, substituted or unsubstituted 5- to 7-membered heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;

wherein if A is substituted with more than one R^1, then each R^1 is optionally different;

wherein if the pyridine ring is substituted with more than one R^2, then each R^2 is optionally different;

wherein if B is substituted with more than one R^3, then each R^3 is optionally different;

wherein two R^1 groups together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7-membered ring;

wherein two R^2 groups together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7-membered ring;

wherein two R^3 groups together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7-membered ring;

wherein R^1 and R^2 together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^2 and R^4 together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^2 and R^5 together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^2 and R^3 together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^1 and X together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^2 and X together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^2 and Y together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring; and

wherein R^3 and Y together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring.

2. The compound of claim **1**, wherein B is selected from substituted or unsubstituted pyridinyl, substituted or unsubstituted 1,2,4-thiadiazole, substituted or unsubstituted pyrimidinyl, substituted or unsubstituted pyrazinyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted isoxazolyl, and substituted or unsubstituted pyrazolyl.

3. The compound of claim **1**, wherein B is substituted or unsubstituted pyridine.

4. The compound of claim **3**, wherein Z^1 is $\overset{\displaystyle -C-}{\displaystyle \|}$ and Z^2 is -N=.

5. The compound of claim **1**, wherein Y is $-NR^5-$.

6. The compound of claim **5**, wherein R^5 is H.

7. The compound of claim **1**, wherein X is a bond.

8. The compound of claim **7**, wherein A is selected from substituted or unsubstituted pyridinyl, substituted or unsubstituted pyrimidinyl, substituted or unsubstituted pyrazinyl, substituted or unsubstituted pyridazinyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted isothiazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted pyrazolyl, and substituted or unsubstituted 1,2,4-oxadiazolyl.

9. The compound of claim **8**, wherein A is selected from substituted or unsubstituted pyridinyl, substituted or unsubstituted pyrazinyl, substituted or unsubstituted thiazolyl, and substituted or unsubstituted pyrazolyl.

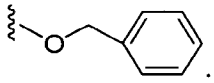
10. The compound of claim **9**, wherein A is selected from unsubstituted pyridinyl, unsubstituted pyrazinyl, unsubstituted thiazolyl, unsubstituted pyrazolyl, and unsubstituted N-methyl pyrazolyl.

11. The compound of claim **1**, wherein R^1 is selected from H, OR^6, NR^7R^8, NO_2, halogen, substituted or unsubstituted (C_1-C_5) alkyl, substituted or unsubstituted 1- to 5-membered heteroalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl.

12. The compound of claim **11**, wherein R^1 is selected from H, NH_2, Br, F, Cl, CF_3, methyl, $-OCH_3$, $-NH-C(O)-CH_3$, $-NH-C(O)-CH_2CH_3$ and morpholinyl.

13. The compound of claim **1**, wherein k is 0.

14. The compound of claim **1**, wherein R^2 is selected from Cl, F, OH, NH_2, substituted or unsubstituted alkyl, and substituted or unsubstituted heteroalkyl.

15. The compound of claim **14**, wherein said substituted or unsubstituted alkyl is (C_1-C_6) alkyl, and said substituted or unsubstituted heteroalkyl is $-CF_3$, $-OCH_3$, $-OCH(CH_3)_2$, $-OCH_2CH_2OCH_3$, $-CH_2C(O)OCH_3$,$-OCH_2C(O)OCH_3$, $-C(O)N(CH_3)_2$, -CN, $-NHC(O)CH_3$, and  .

16. The compound of claim **1**, wherein R^3 is selected from H, OH, NH_2, NO_2, $-SO_2NH_2$, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted (C_5-C_7) cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl.

17. The compound of claim **16**, wherein said substituted or unsubstituted heteroaryl is selected from substituted or unsubstituted pyrrolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted pyrrolidinonyl, substituted or unsubstituted pyridinyl, substituted or unsubstituted thiophenyl, substituted or unsubstituted furanyl, substituted or unsubstituted isoquinolinyl, and substituted or unsubstituted dihydroquinolinyl.

18. The compound of claim **16**, wherein said substituted or unsubstituted 5- to 7- membered heterocycloalkyl is selected from substituted or unsubstituted morpholinyl, substituted or unsubstituted morpholino-, substituted or unsubstituted pyrrolidinyl, substituted or unsubstituted pyrrolidinonyl, substituted or unsubstituted piperidinyl, substituted or unsubstituted piperazinyl, substituted or unsubstituted tetrahydrofuran, substituted or unsubstituted tetrahydropyran, substituted or unsubstituted tetrahydrothiophene, and substituted or unsubstituted tetrahydrothiopyran.

19. The compound of claim **16**, wherein said heteroalkyl is selected from $-L^1OR^8$, $-L^2NR^9R^{10}$, $-L^3C(O)NR^{11}R^{12}$, $-L^4C(O)OR^{13}$, $-L^5C(O)R^{14}$,

wherein

R^8 is selected from H, substituted or unsubstituted (C_1-C_6) alkyl, substituted or unsubstituted 1- to 6- membered heteroalkyl, substituted or unsubstituted 5- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted aryl;

R^9 and R^{10} are independently selected from H, substituted or unsubstituted (C_1-C_6) alkyl, substituted or unsubstituted 1- to 6- membered heteroalkyl, and substituted or unsubstituted heteroaryl;

wherein R^9 and R^{10} together with the nitrogen to which they are joined optionally form a 5- to 7- membered ring;

R^{11} and R^{12} are independently selected from H, substituted or unsubstituted (C_1-C_6) alkyl, substituted or unsubstituted 1- to 6- membered heteroalkyl, and substituted or unsubstituted heteroaryl;

wherein R^{11} and R^{12} together with the nitrogen to which they are joined optionally form a 5- to 7- membered ring;

R^{13} is selected from H, substituted or unsubstituted (C_1-C_6) alkyl, substituted or unsubstituted 1- to 6- membered heteroalkyl, substituted or unsubstituted 5- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted aryl;

R^{14} is selected from H, substituted or unsubstituted (C_1-C_6) alkyl, substituted or unsubstituted 1- to 6- membered heteroalkyl, substituted or

unsubstituted 5- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted aryl; and

L^1, L^2, L^3, L^4 and L^5 are independently selected from a bond, -NH-, and substituted or unsubstituted (C_1-C_6) alkylene.

20. The compound of claim **19**, wherein

R^8 is selected from H, unsubstituted (C_1-C_4) alkyl, $-CH_2CH_2N(CH_3)_2$, and benzyl;

R^9 and R^{10} are independently selected from H, methyl, $-C(O)CH_3$ and pyridinyl;

wherein R^9 and R^{10} together with the nitrogen to which they are joined optionally form an unsubstituted pyrrolidine ring;

R^{11} and R^{12} are independently selected from H and ethyl;

R^{13} is selected from H, methyl and ethyl;

R^{14} is selected from H and methyl;

L^1 is selected from a bond, methylene, ethylene, and propylene;

L^2 is selected from a bond, methylene, and ethylene;

L^3 is a bond;

L^4 is selected from a bond and ethylene;

L^5 is a bond;

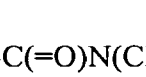
said unsubstituted (C_1-C_7) alkyl is selected from methyl, ethyl, hexyl, isopropyl, isopropenyl, and isobutyl;

said substituted (C_1-C_7) alkyl is CF_3;

said substituted pyridinyl is substituted with at least one pyridinyl substituent, wherein said pyridinyl substituent is selected from methyl, I, Cl, F, $-OCH_2CH_3$ and unsubstituted thiazolyl;

said substituted phenyl is substituted with at least one phenyl substituent, wherein said phenyl substituent is selected from F, $-N(CH_3)_2$ and $-OCH_3$; and

said substituted piperidinyl, substituted piperazinyl and substituted furanyl are each substituted with a methyl.

21. The compound of claim **20**, wherein said heteroalkyl is $-OCH_3$, $-OCH_2CH_3$,  , $-C(=O)N(CH_3)_2$, $-C(=O)OCH_3$, $-(CH_2)_2C(=O)OCH_2CH_3$, $-CH_2OH$, $-(CH_2)_2OH$, $-(CH_2)_3OH$, and $-N(CH_3)(CH_2CH_2OCH_3)$.

22. The compound of claim **1**, wherein R^4 and R^5 are members independently selected from H, substituted or unsubstituted alkyl, and substituted or unsubstituted heteroalkyl.

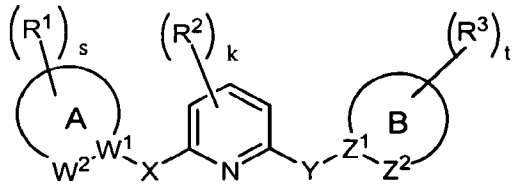
23. The compound of claim **22**, wherein R^4 and R^5 are independently selected from H, substituted or unsubstituted (C_1-C_6) alkyl, substituted or unsubstituted 1- to 6- membered heteroalkyl, and substituted or unsubstituted 5- to 7- membered heteroaryl.

24. The compound of claim **23**, wherein R^4 and R^5 are independently selected from H, methyl, $-C(O)OC(CH_3)_3$, $-C(O)CH_3$, and pyridinyl.

25. A metal complex, comprising a polyvalent metal ion and a polydentate component of a metal ion chelator, wherein said polydentate component is a compound according to claim **1**.

26. The complex of claim **25**, wherein said polyvalent metal ion is selected from iron, zinc, copper, cobalt, manganese, and nickel.

27. A method of decreasing ion flow through potassium ion channels in a cell, said method comprising contacting said cell with a potassium ion channel-modulating amount of a compound of Formula I:



(I)

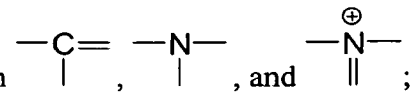
wherein

A and B are independently selected from substituted or unsubstituted 5- or 6-membered heterocyclic and heteroaryl rings,

wherein

W^1 is selected from $-\overset{|}{C}=$ and $-\overset{|}{N}-$;

W^2 is selected from -CH=, -NH-, -N=, and -O-;

Z^1 is selected from  ;

Z^2 is selected from -CH=, -NH-, -N=, and -O-;

X is selected from a bond and $-NR^4-$;

Y is selected from a bond and $-NR^5-$;

s and t are integers independently selected from 1-5;

k is an integer selected from 0-3;

R^2 is independently selected from OR^6, NR^7R^8, NO_2, $-SO_2NR^7R^8$, cyano, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted 3- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;

R^1, R^3, R^4, and R^5 are independently selected from H, OH, NH_2, NO_2, $-SO_2NH_2$, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted 3- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;

wherein if A is substituted with more than one R^1, then each R^1 is optionally different;

wherein if the pyridine ring is substituted with more than one R^2, then each R^2 is optionally different;

wherein if B is substituted with more than one R^3, then each R^3 is optionally different;

wherein two R^1 groups together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein two R^2 groups together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein two R^3 groups together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7-membered ring;

wherein R^1 and R^2 together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^2 and R^4 together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^2 and R^5 together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^2 and R^3 together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^1 and X together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

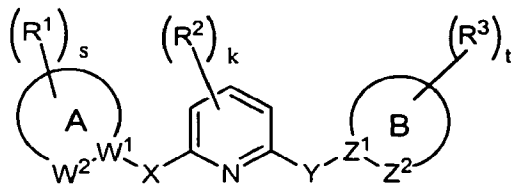
wherein R^2 and X together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^2 and Y together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring; and

wherein R^3 and Y together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring.

28. The method according to claim **27**, wherein said potassium ion channel comprises at least one SK subunit.

29. A method of treating a disease through modulation of a potassium ion channel, said method comprising administering to a subject in need of such treatment, an effective amount of a compound having Formula I:

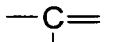
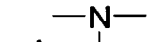


(I)

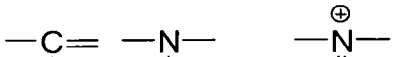
wherein

A and B are independently selected from substituted or unsubstituted 5- or 6-membered heterocyclic and heteroaryl rings,

wherein

W^1 is selected from  and  ;

W^2 is selected from -CH=, -NH-, -N=, and -O-;

Z^1 is selected from  ;

Z^2 is selected from -CH=, -NH-, -N=, and -O-;

X is selected from a bond and $-NR^4-$;

Y is selected from a bond and $-NR^5-$;

s and t are integers independently selected from 1-5;

k is an integer selected from 0-3;

R^2 is independently selected from OR^6, NR^7R^8, NO_2, $-SO_2NR^7R^8$, cyano, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted 3- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;

R^1, R^3, and R^5 are independently selected from H, OH, NH_2, NO_2, $-SO_2NH_2$, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted 3- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;

wherein if A is substituted with more than one R^1, then each R^1 is optionally different;

wherein if the pyridine ring is substituted with more than one R^2, then each R^2 is optionally different;

wherein if B is substituted with more than one R^3, then each R^3 is optionally different;

wherein two R^1 groups together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7-membered ring;

wherein two R^2 groups together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7-membered ring;

wherein two R^3 groups together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7-membered ring;

wherein R^1 and R^2 together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^2 and R^4 together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^2 and R^5 together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^2 and R^3 together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^1 and X together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^2 and X together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

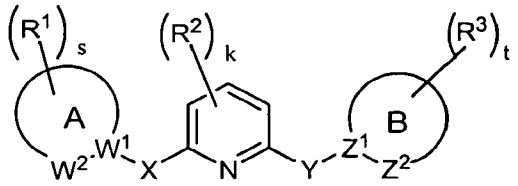
wherein R^2 and Y together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring; and

wherein R^3 and Y together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring.

30. The method according to claim **29**, wherein said disorder or condition is selected from central or peripheral nervous system disorders, neuroprotective agents, gastroesophogeal reflux disorder, gastrointestinal hypomotility disorders, irritable bowel syndrome, secretory diarrhea, asthma, cystic fibrosis, chronic obstructive pulmonary disease, rhinorrhea, convulsions, vascular spasms, coronary artery spasms, renal disorders, polycystic kidney disease, bladder spasms, urinary incontinence, bladder outflow obstruction, ischemia, cerebral ischemia, ischemic heart disease, angina pectoris, coronary heart disease, Reynaud's disease, intermittent claudication, Sjorgren's syndrome, arrhythmia, hypertension, myotonic muscle dystrophia, xerostomi, diabetes type II, hyperinsulinemia, premature labor, baldness, cancer, and immune suppression.

31. The method according to claim **30**, wherein said central or peripheral nervous system disorder comprises migraine, ataxia, Parkinson's disease, bipolar disorders, trigeminal neuralgia, spasticity, mood disorders, brain tumors, psychotic disorders, myokymia, seizures, epilepsy, hearing and vision loss, psychosis, anxiety, depression, dementia, memory and attention deficits, Alzheimer's disease, age-related memory loss, learning deficiencies, anxiety, traumatic brain injury, dysmenorrhea, narcolepsy and motor neuron diseases.

32. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of Formula I:



(I)

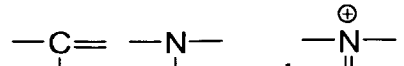
wherein

A and B are independently selected from substituted or unsubstituted 5- or 6-membered heterocyclic and heteroaryl rings,

wherein

W^1 is selected from $-C=$ and $-N-$;

W^2 is selected from -CH=, -NH-, -N=, and -O-;

Z^1 is selected from  ;

Z^2 is selected from -CH=, -NH-, -N=, and -O-;

X is selected from a bond and $-NR^4-$;

Y is selected from a bond and $-NR^5-$;

s and t are integers independently selected from 1-5;

k is an integer selected from 0-3;

R^2 is independently selected from OR^6, NR^7R^8, NO_2, $-SO_2NR^7R^8$, cyano, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted 3- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;

R^1, R^3, R^4, and R^5 are independently selected from H, OH, NH_2, NO_2, $-SO_2NH_2$, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted 3- to 7- membered cycloalkyl, substituted or unsubstituted 5- to 7- membered heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;

wherein if A is substituted with more than one R^1, then each R^1 is optionally different;

wherein if the pyridine ring is substituted with more than one R^2, then each R^2 is optionally different;

wherein if B is substituted with more than one R^3, then each R^3 is optionally different;

wherein two R^1 groups together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7-membered ring;

wherein two R^2 groups together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7-membered ring;

wherein two R^3 groups together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7-membered ring;

wherein R^1 and R^2 together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^2 and R^4 together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^2 and R^5 together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^2 and R^3 together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

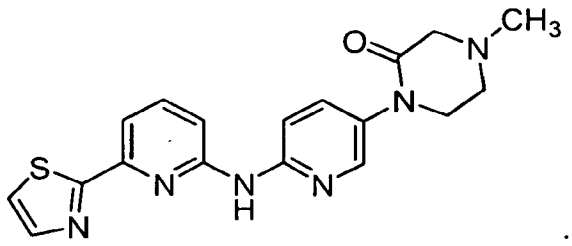
wherein R^1 and X together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

wherein R^2 and X together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring;

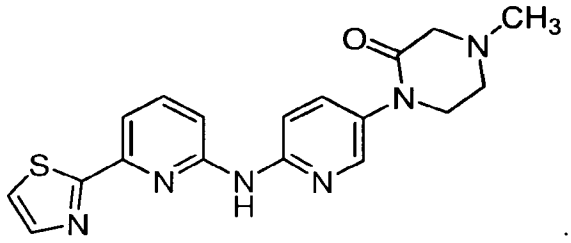
wherein R^2 and Y together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring; and

wherein R^3 and Y together with the atoms to which they are joined optionally form a substituted or unsubstituted 5- to 7- membered ring.

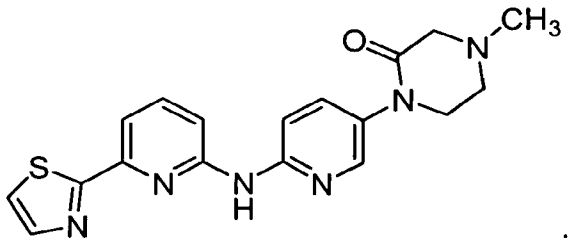
33. A compound having the formula:



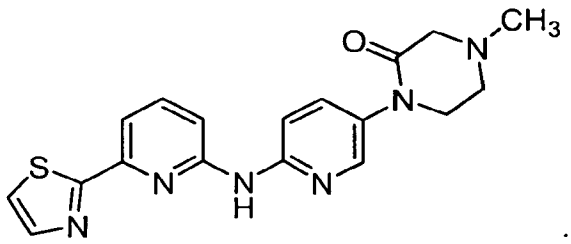
34. A method of decreasing ion flow through potassium ion channels in a cell, said method comprising contacting said cell with a potassium ion channel-modulating amount of a compound of the formula:



35. A method of treating a disease through modulation of a potassium ion channel, said method comprising administering to a subject in need of such treatment, an effective amount of a compound having the formula:



36. A composition comprising a pharmaceutically acceptable excipient and a compound of the formula:



PYRIDINYL AMINES AS POTASSIUM ION CHANNEL MODULATORS

ABSTRACT OF THE DISCLOSURE

The present invention provides a genus of pyridinyl amines that are useful as modulators of potassium ion channels. The compounds of the invention are of use in both therapeutic and diagnostic methods.

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Application Data Sheet

Application Information

Application number::	
Filing Date::	04/13/04
Application Type::	Provisional
Subject Matter::	Utility
Suggested classification::	
Suggested Group Art Unit::	
CD-ROM or CD-R??::	
Number of CD disks::	
Number of copies of CDs::	
Sequence Submission::	
Computer Readable Form (CRF)?::	
Number of copies of CRF::	
Title::	PYRIDINYL AMINES AS POTASSIUM ION CHANNEL MODULATORS
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Request for Early Publication::	No
Request for Non-Publication::	No
Suggested Drawing Figure::	0
Total Drawing Sheets::	0
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Latin name::	
Variety denomination name::	
Petition included?::	No
Petition Type::	
Licensed US Govt. Agency::	
Contract or Grant Numbers One::	
Secrecy Order in Parent Appl.::	No

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Representative Information

Representative Customer Number:: 20350

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Foreign Priority Information

Country::	Application number::	Filing Date::

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